1. Molecular Effects of Some Nonsteroidal Anti-Inflammatory Drugs

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Anti-inflammatory drugs produce cytostatic effects on cell cultures and haematopoietic systems, probably by interfering with DNA and RNA synthesis. We have studied DNA and RNA content of edema tissue in acute inflammation (carrageenin and formaldehyde edema) and chronic inflammation (cotton pellet granuloma, granuloma pouch and Fraunds' adjuvant arthritis) in rats, and seen the effects of nonsteroidal anti-inflammatory drugs. The results will be discussed.

2. Histamine Receptors in Capillary Permeability

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A well known effect of histamine is to increase capillary permeability. However, the nature of the receptor involved in this action of histamine has not yet been identified. With the availability of specific H₁ and H₂-receptor agonist and antagonists, it is now possible to assess the histamine receptors involved in this effect. The present study employed the estimation of peritoneal diffusion of Evan's blue dye as a measure of capillary permeability in albino mice. Histamine and 2-methyl histamine (H₁-receptor agonist) markedly increased the capillary permeability while 4-methyl histamine (H₂-receptor agonist) cause insignificant increase. Mepyramine (H₁-receptor antagonist) pretreatment significantly blocked the effect of histamine and 2-methyl histamine. Burimamide (H₂-receptor antagonist) afforded insignificant protection to histamine induced increase in capillary permeability. Moreover, combined mepyramine and burimamide pretreatment did not show any significantly greater protection against histamine induced increase in capillary permeability when compared with that obtained with mepyramine alone. These experiments suggested that histamine-induced increase in capillary permeability is mediated through the H₁-receptors.
3. Anti-inflammatory and Anti-arthritic Activity of Calophyllolide: a Natural Coumarine Derivative

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Anti-inflammatory activity has been reported in various active principles obtained from indigenous plants like glycyrrhetic acid, oleoresins and α and β amyrin-acetate. Preliminary screening of various natural plant coumarine and triterpenoids showed a promising anti-inflammatory activity in calophyllolide. The present study was undertaken to further evaluate the anti-inflammatory and anti-arthritic activity of calophyllolide using various models as well as the safety evaluation of the compound. Initial study of calophyllolide in carrageenin induced oedema revealed an ED50 of 140 mg/kg. Subsequently this dose was employed in formaldehyde induced arthritis, cotton pellet implantation method as well as in adjuvant arthritic rats. Hydrocortisone served as a reference standard. The compound showed potent anti-inflammatory and anti-arthritic activity comparable to that of hydrocortisone. LD50 of the compound was found to be more than 2.5 gm/kg p. o. in albino mice. The subacute toxicity studies showed no reduction in the weight of the animals and revealed no histopathological changes in the vital organs. The compound seems to hold a good promise in future and is under further evaluation.

4. Local Anti-inflammatory Effect of Curcumin, Sodium curcuminate and Phenybutazone

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The anti-inflammatory activity of curcumin and its semisynthetic analogues in carrageenin induced rat paw edema after oral administration was earlier reported from this laboratory. In the present study the effect of injecting curcumin, sodium curcuminate and phenylbutazone alone with irritants like carrageenin and kaolin into the rat paw has been investigated. Sodium curcuminate and curcumin produced 93 and 67% inhibition of inflammation at 1 mg dose six hour, after kaolin injection. However, the activity decreased to 58 and 47% respectively at 3 mg dose. Phenylbutazone showed dose dependent response in all the doses studied with a maximum anti-inflammatory activity of 87% at 3 mg dose. In similar experiment using carrageenin es irritant sodium curcuminate increased the inflammation to 21.5% at 3 mg dose although curcumin retained 31% anti-inflammatory activity. The activity of phenylbutazone at 3 mg was 84% which
is close to that of kaolin method. When sodium curcuminate and phenylbutazone were applied locally in the cotton pellets, sodium curcuminate produced 14% inhibition of granuloma tissue growth at 0.1 mg dose. However the growth of granuloma tissue increased with higher doses. Phenylbutazone was effective in inhibiting granuloma tissue growth in all the doses studied. The significance of the results will be discussed.

5. Anti-inflammatory Study of Aloe Barbadensis Along with other Studies
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Hydroalcoholic extract of Aloe Barbadensis was obtained. Anti-inflammatory activity of this extract was studied by the inflammation produced by formalin and dextran solution in the hind paw of rats. The effect of this extract was also studied on the blood pressure, respiration of anaesthetised mammal. Its effects were also studied on the normal intestinal movement of rabbit along with acetylcholine and barium induced stimulation of intestine. The drug was found to be possessing moderate anti-inflammatory action and did not show any significant effect on other pharmacodynamic studies. All these effects of aloe barbadensis will be discussed.

6. Further Studies on the Anti-inflammatory Activity of a Bioflavonoid Gossypin
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The anti-inflammatory activity of some bioflavonoids including gossypin has been reported by us earlier. The present report deals with the elucidation of the mechanism of action of gossypin. It has been studied alone and in combination with the non-steroid anti-inflammatory agents, ascorbic acid, adrenaline, propranolol, phentolamine and in the adrenalectomized rats against carrageenin-induced paw oedema. Its effect has also been investigated against the increase in vascular permeability and paw oedema induced by some well established mediators of inflammation like histamine, 5-HT, bradykinin, \( \text{PGE}_2 \) and hyaluronidase. Lastly, its effect has been studied on the migration of leucocytes in the carrageenin and turpentine-induced pleurisy in rats. The results and significance of these observations will be discussed.
7. Studies on the Anti-Inflammatory Effect of Blumea Lacera in Rat

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Blumea Lacera is an indigenous plant. Preliminary studies were carried out for the possible anti-inflammatory activity of the alcoholic extract of blumea lacera plant, on some acute and chronic models of inflammation. Acute oedema of rat hind paw was produced by carrageenin (1%). dextran (6%), 5-hydroxytryptamine (1 mg/ml), bradykinin (10μg/ml). Chronic tests were performed with granuloma pouch and cotton pellet implantation techniques. The extract showed significant anti-inflammatory effect against bradykinin induced oedema but was ineffective against 5-HT and dextran induced oedema. It had insignificant effect against carrageenin induced oedema. It had significant anti-inflammatory effect against granuloma pouch and cotton pellet implantation but less potent than that of phenylbutazone and betamethasone. It had no ulcerogenic property on gastric mucosa. Its anti-bradykinin activity may be one of the factors responsible for its anti-inflammatory activity.

8. Studies on the Involvement of Autacoids in Diethylcarbamazine Induced Reaction in Filariasis

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Administration of diethylcarbamazine (DEC) to microfilaraemic patients is often followed by reaction, i.e., flushing, urticaria, fever and bodyache. The present investigation was undertaken to explore the possible involvement of histamine, 5-hydroxytryptamine and bradykinin in the reaction induced by DEC in microfilaraemic patients. Samples of venous blood were drawn from microfilaraemic patients on days 0, 2 and 8; DEC was administered on day 0. A control group of healthy persons were administered DEC and sampled in parallel. Blood samples were estimated for histamine, 5-hydroxytryptamine and bradykinin content. Amongst microfilaraemic patients showing DECR, there was a distinct and temporary rise in the level of histamine and bradykinin (but not 5-hydroxy-tryptamine). In patients without reaction, as well as in healthy patients, there was no rise in the level of histamine, 5-hydroxytryptamine or kinin. The rise of histamine and kinin levels in DECR suggests the possibility of involvement of these autacoids in the reaction process.
9. Influence of Various Nonsteroidal Anti-inflammatory Agents on Effects of Warfarin Sodium

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Coumarin derivatives are frequently employed as anticoagulants in various thromboembolic disorders. Warfarin sodium, a coumarin derivative has a high degree of protein binding. It is likely that when agents like non-steroidal anti-inflammatory agents having similar affinity for protein binding are employed in therapy along with warfarin sodium they can displace it from the protein binding sites leading to higher levels of free warfarin sodium. The present study was therefore undertaken to evaluate the influence of different non-steroidal anti-inflammatory agents on effects of warfarin sodium, namely effect on prothrombin time in rats and effect on platelet aggregation in vitro using human blood. This was particularly to find out if any of these agents can safely be employed for some painful disorder in a patient who is on oral anticoagulant therapy. Results will be discussed.

10. Studies on the Effects and Probable Mechanism of Action of Prostaglandins on Tissue Mast Cells

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A regulatory role for thymus on tissue mast cells has been suggested earlier. Many workers have attributed regulatory roles to several hormones and prostaglandins on tissue mast cells. With a view to correlate the various findings the effects of prostaglandins $E_2$ and $F_2$ alpha on tissue mast cells were studied in detail. Prostaglandin $E_2$ and $F_2$ alpha were administered in adult Wistar albino rats after thymic suppression with betamethasone, thymectomy and after adrenalectomy. Prostaglandins ordinarily produce a slight increase and marked degranulation of mast cells in the mesentery. In thymectomised rats prostaglandins $E_2$ and $F_2$ alpha produced only degranulation of tissue mast cells while in adrenalectomised rats only a slight increase in number. In betamethasone treated rats, prostaglandins induced a marked degranulation and slight increase in tissue mast cell numbers. In rats subjected to both thymectomy and adrenalectomy, there was no significant change in tissue mast cells. Tissue spreads containing mast cells treated in vitro with prostaglandins and betamethasone confirmed the in vivo studies. The significance of these results will be discussed.
11. Possible Mechanism of Histamine Induced Blanching in Frogs

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Histamine produces dose dependent (250 μg-2mg injected in dorsal lymph sac) blanching of skin colour and corresponding reduction in melanophore index (M.I.) in normal frogs. The maximum effect was observed with a dose of 2 mg. Histamine releasers like d-tubocurarine and octylamine also produced blanching response. This effect of histamine was completely blocked by mepyramine (1 mg) and chlorpheniramine (100 μg). The effect was also blocked by phenoxybenzamine (1 mg) and propranolol (200 μg). In reserpinized (1 mg) frogs histamine failed to produce blanching but noradrenaline did produce blanching. Pinealectomy had no effect on histamine induced blanching. In decapitated frogs histamine (2-5 mg) could not produce its maximum blanching response. In decapitated frogs lower doses of mepyramine (200 μg) and phenoxybenzamine (200 μg) were required to block histamine response completely.

12. Mechanism of Histamine Induced Experimental Broncho-constriction in the Guinea pig

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Broncho-constriction is a characteristic feature of clinical pathophysiology of bronchial asthma. A wide variety of pharmacological agents including histamine, induce broncho-constriction under experimental conditions either due to their direct action on the bronchial musculature or indirectly through secretory and reflex mechanisms. Classical antihistaminics have been shown to considerably antagonise histamine induced bronchospasm. With the availability of newer specific H₂-receptor antagonists, it was thought worthwhile to investigate the nature of histamine receptors involved in the broncho-constriction induced by histamine aerosol in guinea pigs. The results showed that mepyramine (H₁-receptor antagonist) and burimamide or metiamide (H₂-receptor antagonists) either alone or combined, afforded approximately 70% protection against histamine induced bronchospasm in guinea-pigs. It may, therefore, be concluded that whereas both H₁ and H₂ receptors are involved in the histamine-aerosol induced experimental broncho-constriction in guinea pigs, the total broncho-constrictor action of histamine cannot be explained entirely on the basis of H₁ and H₂ receptors.
Histamine concentration has been reported to be 177 ng/gm in rat hypothalamus. It has also been found that turnover rate of portion of brain histamine is very rapid. Role of histamine in thermoregulation is not well elucidated. In the present study an attempt has been made to find out possible role of histamine on thermoregulation in rat. Intracerebroventricular (ICV) injection of drugs in a volume of 0.025 ml were carried out under light ethyl chloride anaesthesia. In order to check actions of systemically absorbed drugs from ICV injection suitable antagonists were administered intraperitoneally (I. P.). The rectal temperature of the animals was recorded by means of electronic thermometers under controlled room temperature. Histamine (25 and 125 µg, ICV) was found to be hypothermic. 2-Methyl histamine (25 and 125 µg, ICV) showed insignificant effect but 4-methyl histamine (125 µg, ICV) showed significant and persistent fall in body temperature. Further experiments were carried out with histamine agonists (ICV and IV) and/or antagonists (ICV and IP). The role of H₁ and H₂ receptors in thermoregulation and their interaction will be discussed.

Histamine liberators cause vasodilatation and hypotension through the release of histamine (mainly) from mast cells. The frog blood vessels, however, showed constriction after histamine liberators while histamine itself did not produce significant effect. Similarly effect of the compound 48/80 on the frog heart was not by H₁ and H₂ blockers. But the rapid tachyphylaxis indicates that something is released by them. As a first step to find the answer to this question it was decided to look for the mast cells in the frog and attempt at correlation of the mast cell behaviour to the vasoconstrictor responses. Therefore, the search for mast cells was made and the morphology was studied, and compared with that of rats. The effects of camp. 48/80 was studied by (a) in vitro challenge and (b) in vivo exposure in perfusion experiments on coeliacomesenteric vascular bed. In the former the tissue was stained 10 min after the exposure to the camp. 48/80 and in the latter 5 min after the peak constrictor response. The results will be discussed.
15. The Probable Mechanism of the Hyperglycaemic Action of Prostaglandins \( \text{E}_2 \) and \( \text{F}_3 \) Alpha
   
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Prostaglandins \( \text{E}_2 \) and \( \text{F}_3 \) alpha produce hyperglycaemia in rats, rabbits and dogs. Studies were conducted in: (1) Adrenalectomized rats and dogs, (2) Adrenal demedullated rats, (3) Adrenalectomized-depancreatized rats and dogs, in order to try to elucidate the probable mechanism of hyperglycaemic action. \( \text{PGE}_2 \) and \( \text{PGF}_\alpha \) were administered in the dose of 1 mg/kg body weight subcutaneously, separately to each group of animals. A mild and almost similar increase in blood glucose was observed in all the three groups when compared to the adrenal and pancreas intact animals. Hence, we infer that the hyperglycaemic action is probably mediated mostly through the adrenal medulla and partly through an extra adrenal extrapancreatic component-probably a direct glycogenolytic action on the liver.

16. Sodium Nitroprusside and Non-Vascular Smooth Muscles

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The drug sodium nitroprusside appears uniquely specific for vascular smooth muscle. Is it really specific for vascular smooth muscle? An off-hand answer is difficult; there are scanty reports about the effect of nitroprusside on other smooth muscle. Since, the therapeutic prospects of nitroprusside has increased of late it is desirable to have information about its various pharmacologic effects. This in view, we have studied the effects of this drug on smooth muscles other than vascular. For the purpose, we have utilized ileum, tracheal chain, uterus and tracheo-bronchial tree of guinea-pig, and colon, uterus and fundus (two types of preparations) of rat. The drug has been tested for its direct effect and also for its influence on the agonists like acetylcholine, histamine, serotonin and barium chloride. The interesting findings are (a) The drug directly relaxes tracheal and fundal smooth muscle & also antagonises all the agonists used in these preparations. (b) It does not cause relaxation of ileal, uterine and colonic smooth muscle, in fact, it caused contraction in some of the preparations. In all these tissues it did not antagonise acetylcholine, some times it potentiated. Other agonists like histamine, serotonin and bariumchloride were antagonised significantly. These surprising and varying behaviours of nitroprusside (in doses ranging from 0.15 to 12 mcg/ml) have been analysed.
17. Effect of Stress on Blood Pressure and Heart Rate Responses to Catecholamines and Acetylcholine in Albino Rats
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Studies were conducted to investigate the affects of stress on blood pressure (B. P.) and heart rate (H. R.) responses to adrenaline (AD), nor-adrenaline (NA) and acetylcholine (ACh) in dosage of 5-20 μg/kg, i. v. each in albino rats of either sex weighing between 150-250 G. Stress was induced by foot electric shock (70 V, 72/min of 10 millisec, total 15 min). Rats were given either one exposure (Acute stress-AS) or one exposure every day for seven days (Chronic stress-CS). After 15 min or 24 hr of AS or CS, rats were anaesthetised with pentobarbitone sodium 40 mg/kg, i. p, and the cardio-vascular responses were recorded. For comparison, effect of hydrocortisone acetate (HC, 2 mg/kg, i. p. 30 min before) and adrenalectomy (ADT, 48 hr before) were also studied. AS, CS and HC produced a slight rise in B. P. and H. R. AS and ADT slightly reduced while HC slightly increased the pressure response to AD and NA, and CS produced no change. AS, CS and HC had no effect but ADT reduced ACh responses. AS, CS and ADT reduced the reflex negative inotropic effect of AD and NA while HC had no consistent effects. AS, CS and HC increased the negative inotropic effect of ACh. The results will be discussed.

18. Effect of Anticholinesterase Agents on Isoprenaline Induced Ca^{45} Uptake of Rat Heart
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Acetylcholine (ACh) has been reported to inhibit cardiac glycogenolysis by adrenaline and theophylline and to partially inhibit that caused by anoxia in isolated guineapig heart. Physostigmine, an anti-cholinesterase agent, has been found to significantly inhibit cardiac glycogenolysis after light petroleum+
adrenaline and ventricular glycogenolysis after myocardial ischaemia in anaesthetised dogs. Biochemical, functional and structural changes in the heart following high doses of isoprenaline (ISP), a beta-adrenergic stimulant, are known to be related to an increase in trans-membranous influx of Ca++ into the myocardial fibres. Studies were conducted in albino rats of either sex weighing between 80-120 G to elucidate the effect of physostigmine (Ph) and prostigmine (Pr) on ISP induced $\text{Ca}^{45}$ uptake of heart. $\text{Ca}^{45}$ was given 100 microcurie/kg, i. p. and $\text{Ca}^{45}$ uptake of heart and plasma was estimated 6 hr afterwards with the help of gas flow counter. Ph (0.1 mg/kg, i. p.), Pr (0.1 mg/kg, i. p.) and atropine (At-1mg/kg, i. p.) have been administered at 0 hr and at 4 hr, while ISP (30 mg/kg, s. c.) was administered at 0 hr. $\text{Ca}^{45}$ uptake of heart was calculated as % of plasma concentration. ISP increased the $\text{Ca}^{45}$ uptake to 3 folds. Ph, Pr and At have no significant effects. Ph were found to completely antagonise enhanced $\text{Ca}^{45}$ uptake induced by ISP. This action of anticholinesterase agent was found to be antagonised by At. The results show that the anticholinesterase agents inhibit influx of $\text{Ca}^{45}$ induced by isoprenaline into the myocardial fibre and this action is mediated through atropine sensitive receptors.

19. Effect of Adrenergic Blockade on Pulmonary Oedema Induced by Trauma to Skull in Mice-A Preliminary Study

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Pulmonary oedema is encountered in so many clinical conditions. Trauma to skull in man is a common cause of pulmonary oedema if the patient survives for several hours. This clinical condition has been simulated in experimental animals in the present study. It has been suggested that the major changes leading to pulmonary oedema induced by trauma to skull is caused by sympathoadrenal storm. Taking into account the above fact, the effect of different type of adrenergic blockers have been studied. Tolazoline hydrochloride (alpha adrenergic blocker) in the dose of 0.20 mg/20 G of mice intramuscularly (I. M.), propranolol hydrochloride (beta blocker) in the dose of 0.4 mg/20 G of mice I. M., guanethedine hydrochloride (adrenergic neuron blocker) in the dose of 0.13 mg/20 G of mice I. M. were used for the study. For assessing the pulmonary oedema the following parameters were used : 1. Lung Body Index=$\frac{\text{Weight of lung}}{\text{Body weight}}\times100$. 2. Haemorrhage in the lung-by macroscopic observation. The study revealed that propranolol (beta blocker) alone prevented Pulmonary oedema to a significant degree (P<0.05 for L. B. I. and P<0.005 for haemorrhage in the lungs) whereas other adrenergic blockers did not prevent pulmonary oedema.
20. The Effect of Sympathomimetic Amines and Their Blockers on the Rumen Motility of Buffalo Calves

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Epinephrine, nor-epinephrine were investigated for their effects on rumen motility in buffalo calves. The rumen movement were recorded on physiograph by direct puncturing of rumen with needle connected to a transducer. The threshold dose of epinephrine which inhibited the rumen motility was found to be 1 \( \mu g/kg \) end the extent of the inhibition was in a linear fashion with increase in dose up to 10 \( @g/kg \). The threshold dose of norepinephrine and isoprenaline to produce the inhibition of lumen motility was found to be 0.5 and 0.1 \( \mu g/kg \) respectively. The maximal inhibitory effect with norepinephrine and isoprenaline became evident with 10 \( \mu g/kg \) and 5 \( \mu g/kg \) respectively. Dihydro-ergotamine (DHE) was used as en alpha adrenergic blocking agent and it was investigated that DHE in dosage of 20 \( \mu g/kg \) almost completely blocked the inhibitory effect of 10 \( \mu g/kg \) of epinephrine on rumen movements. However, DHE in dosage of 20 \( \mu g/kg \) was required to block the inhibitory effect of norepinephrine (10 \( @g/kg \)). Propranolol, a beta blocking agent in dosage of 0.5 mg/kg was found to block the inhibitory effect of 10 \( \mu g/kg \) epinephrine and 5 \( \mu g/kg \) of isoprenaline.

21. Central Adrenoceptors Concerned with Cardiovascular Regulation

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In \( \alpha \)-chloralose anaesthetised cats, superfusion of posterior hypothalamus or perfusion from lateral ventricle to aqueduct with adrenaline or isoprenaline induced rise of blood pressure and tachycardia. These cardiovascular effects were completely blocked after central administration of sotalol or propranolol. On the other hand, clonidine induced hypotension and bradycardia were antagonized by the central administration of piperoxan. Similar localization of adrenaline or clonidine to the medullary region elicited fall of blood pressure and bradycardia. Clonidine induced responses were blocked by central piperoxan, on the other hand adrenaline induced hypotension end bradycardia was converted into hypertension and tachycardia, which was blocked by central administration of sotalol or propranolol. Isoprenaline localized to the medullary region resulted in hypertension and tachycardia. These responses were again blocked by \( \beta \)-blockers. Intrathecal administration of adrenaline facilitated the spinal compression vasomotor response (SCVR) in spinal transected cats. Piperoxan enhanced the adrenaline induced facilitation of SCVR, whereas, propranolol
effectively blocked the adrenaline induced facilitation of SCVR. Isoprenaline induced facilitation of SCVR was also antagonized by propranolol. Clonidine induced inhibition was blocked by piperoxan. These results demonstrate that β-adrenoceptors all along the neuraxis are facilitatory for cardiovascular control while, α-adrenoceptors are inhibitory in nature.

22. Effect of Different Anesthetics on Pilocarpine Induced Salivation in Rabbits

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Anesthetic agents are known to affect the responses of various drugs. In the present study the influence of different anesthetics on pilocarpine induced salivation was evaluated. 10 Rabbits were employed for each anesthetic, and a crossover design was used. The details of the findings will be discussed.

23. Some Aspects of Ephedrine Tachyphylaxis

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When there is tachyphylaxis to ephedrine after repeated administration, there is-(a) Raised basal level of blood pressure and (b) Pressor response to ephedrine is converted to depressor response. In the first part of the present investigation experiments are conducted to see whether these phenomena are central in origin. The post-tachyphylactic depressor response is present in spinal dogs and further in the post tachyphylactic state when ephedrine is administered I. C. V. and/or intracarotid, the depressor response is absent. In the second part the effects of drugs known to act by influencing central vasomotor controlling areas, are tested after tachyphylaxis to ephedrine is established.


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Dexamphetamine and certain other indirectly acting sympathomimetic amines prevent the sympathetic nerve blocking action of guanethidine in anesthetised cats and dogs. Present study is confined to elucidate the possible mechanism of interaction involved between dexamphetamine and guanethidine on isolated preparations. Results will be discussed.
25. Investigation of Spasmogenic Action of General Anaesthetic Ether in Intestinal Smooth Muscle

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General anaesthetic like ether has been shown to produce relaxant effect on rat uterus, and on bronchial smooth muscle. It is not clear whether ether induced relaxation of these smooth muscle is due to the stimulation of beta adrenergic receptors or a direct nonspecific effect. In view of this, we studied the effect of ether on intestinal smooth muscle to find out the nature of relaxant effect. To our surprise, we did not get relaxant effect. Ether produced contraction of smooth muscle of intestine which was blocked by atropine and also showed tachyphylaxis. After the development of tachyphylaxis, incubation of preparation with acetylcholine restored the spasmogenic response to ether. These observations suggest that spasmogenic effect on intestinal smooth muscle produced by ether is cholinergically mediated and may be due to release of endogenous acetylcholine.

26. Effect of Reserpinisation and Adrenoceptor Blockade on Tissue Glycogen and Blood Glucose Concentration of Albino Rats

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In this study, the tissue glycogen and blood glucose level was studied after administration of low doses of reserpine (15 μg) subcutaneously for 7 consecutive days in one group and induction of dual (Alpha and Beta) adrenoceptor blockade by low doses of phentolamine (0.3 mg/kg, i.m.) and propranolol (0.1 mg/kg, i.v.) in another group. Thirty albino rats weighing between 80-150 G were distributed into three groups. Control studies were conducted with the rats in group I. These of group 2 were injected with 15 μg/kg of reserpine subcutaneously for seven consecutive days and group 3 with 0.3 mg/kg phentolamine i. M. and 0.1 mg/kg. propranolol i. V. The tissue used for glycogen estimation were liver, cardiac muscle (auricle and ventricle and skeletal muscle). Blood glucose estimation was done in all the three groups. Reserpinisation caused marked lowering of glycogen in the myocardium (both chambers), skeletal muscle and marked rise of blood glucose concentration without significantly altering the content of liver glycogen. But dual adrenoceptor blockade caused a significant lowering of blood glucose concentration without altering the glycogen content of any of the tissues.
27. Modification of Bronchodilator Activity of Catecholamines by Alpha Adrenergic Blockers

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We have reported earlier the potentiation of bronchodilator activity of catecholamines by alpha adrenergic blockers on guinea-pig tracheal chain. In the present study a state of poor responsiveness of the tissue to catecholamines has been produced by using acidic Kreb's solution and modification of this state by alpha adrenergic blockers has been studied. The work has also been extended to in vivo experiments using Konzett-Rossler's method. The results of these will be discussed.

28. Effects of Hypothermia and Physostigmine on the Cardiac Acetylcholine and Tissue Glycogen Contents in Frogs in Different Seasons

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Seasonal variations are known to effect physiological functions and metabolism in poikilothermic animals. Studies were conducted in frogs in summer (May-June), rainy seasons (July-Oct.) and winter months (Dec.-Feb.). Acetylcholine contents of heart and glycogen contents of cardiac ventricle, liver and skeletal muscle and blood sugar contents were estimated. Physostigmine (1.0 mg/kg) through the ventral lymph sac was administered one hour before estimations. Frogs were also rendered hypothermic (8°C) by surface cooling method for 2 hr before the estimation. Seasonal variation did not produce any significant change in the cardiac acetylcholine content. There was no significant difference in the tissue glycogen contents during summer and rainy seasons but the tissue glycogen was markedly depleted during winters. Blood sugar was relatively high during rainy seasons. Ph increased the cardiac Ach contents in all seasons but it was significant during winter. Ph did not produce any significant change in the tissue glycogen contents in any seasons except slight decrease in ventricular glycogen during winters and increase in muscle glycogen during summers. Ph also produce hyperglycaemia during rainy and winter months. Hypothermia produced marked reduction in cardiac Ach contents and marked depletion in tissue glycogen contents during summer and rainy seasons. It also produced hyperglycaemia which was more in rainy seasons than in summers. Ph pretreatment increased cardiac Ach contents in hypothermic frogs in summers and rainy seasons. Ph inhibited cardiac glycogenolysis during summers and
rainy seasons and hepatic glycogenolysis during rainy seasons induced by hypothermia. The hyperglycaemic effect of hypothermia was not significantly affected by Ph. The results indicate that physiological and biochemical behaviour of the frogs is affected by seasons.

29. A Study of the Effects of Catecholamines on the Concentration of Blood Glucose in Dogs

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Ten adult healthy dogs weighing between 10 to 15 kg were each injected with 3 ml of normal saline subcutaneously. Samples of blood were collected 1 hour before the injection (−1 hour sample), immediately following injection (0 hour sample) and +1, 2, 3, 4, 5 hours after injection. Blood glucose concentration was estimated and the mean values corresponding to different samples were estimated along with the standard deviations and errors. These were used as the control values. Equimolar doses/kg of epinephrine, norepinephrine and isopropyl-norepinephrine were injected subcutaneously in three other groups (of 10 dogs in each) and blood samples were collected and analysed as above. The catecholamines were found to raise the concentration of blood glucose to different degrees in the samples studied. The result will be discussed and the responses to the three catecholamines compared.

30. A Study of the Effects of Adrenergic Blockade on Catecholamine Induced Change in the Concentration of Blood Glucose in Dogs

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Three groups of adult dogs (ten each) were injected subcutaneously equimolar doses of epinephrine (0.3mg base/kg), norepinephrine (0.28 mg base/kg), isopro- pyl norepinephrine (0.35 mg/kg) respectively. Blood samples were collected 1 hour before injection (−1 hour sample), immediately after injection (0 hour sample) and +1, 2, 3, 4, 5 hours after injection and the blood glucose concentration was estimated. The mean concentration of blood glucose after
the catecholamines were compared with the control values obtained in the corresponding samples collected from a group of ten dogs in which normal saline has been injected subcutaneously at ‘0’ hour. Alpha, beta and dual adrenoceptor blockade were induced in three groups of (ten) dogs with subcutaneous injection of phentolamine, propranolol and phentolamine followed by propranolol respectively at −½ hours. The collection of blood samples and the estimation of the concentration of blood glucose was done as in the control study and their means served as basal levels for the subsequent part of the study. Equimolar doses of the three catecholamines were injected as before into three other groups of adrenoceptor-blocked dogs and the concentration of blood glucose in the samples was estimated. The responses to the three catecholamines in adrenoceptor-blocked dogs are compared with the responses to them in normal dogs. The observation will be discussed.

31. Adrenotropic Receptors in Rabbit Intestine
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Studies on the canine ileum and on the rabbit intestine have presented evidence that the intestinal relaxations of sympathomimetic amines (SMAs) can be the result of stimulation either of alpha or of beta adrenotropic receptors. The differential susceptibility of the SMAS to blockade with alpha and beta adrenoceptor antagonists in the intestine have been shown to be consistent with the above concept. The purpose of this study is to find relative quantitative potencies of different SMAs in terms of intrinsic activity \( i.e., (I) \) and affinity \( pD_2 \), and the quantitative adrenergic antagonism \( pA_2 \) on the rabbit intestine. The relaxant effect of four SMAs, viz., epinephrine (E), norepinephrine (NE), phenylephrine (PE) and isoproterenol (IP) were studied on isolated rabbit jejunum. The i. a. and \( pD_2 \) of the agonists and \( pA_2 \) of the antagonists-an alpha adrenoceptor blocker phentolamine (PTA) and a beta adrenoceptor blocker bunolol (B) have been determined. The i. a., of all the SMAs were more or less equal in inducing the maximum response, but the affinity of PE towards receptor sites was less (i.e., low \( pD_2 \) values). The antagonism of PE response by PTA and IP response by B were more specific as compared to other combinations. The results indicate that the relaxant effects of PE and IP are predominantly mediated through alpha and beta adrenoceptors respectively, while those of E and NE are mediated through both types of receptors.
32. **A Study of the Effects of Adrenergic Blockade on the Basal Blood Glucose Concentration in Dogs**

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The adult healthy dogs were injected with three ml of normal saline subcutaneously and blood samples were collected ½ hour before the injection (−½ hour sample), immediately after injection (0 hour sample) and 1, 2, 3, 4, 5 hours after injection. The glucose concentration in each sample was estimated and the mean of values corresponding to each sample along with their standard deviation and errors were estimated and used as control values for the subsequent part of this study. Alpha and beta-adrenoceptor blockade were induced in two groups (10 dogs X 2) by injection of 8 mg/kg of phentolamine and 2 mg/kg of propranolol respectively at −½ hour and dual adrenoceptor blockade in a third group by phentolamine followed by propranolol at −½ hour. Blood samples were collected as in the control study, the concentrations estimated and mean values with S. D. and S. E. determined as before. Significant reduction of basal blood glucose level was observed after all three types of adrenoceptor blockade and was most marked after dual blockade. The effects of the three types of blockade on the basal blood glucose level will be compared and discussed.

33. **Role of α and β Receptors in Carbohydrate Metabolism During Thermal Stress**

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The involvement of autonomic nervous system during stress is well known, but the role played by α and β receptors in carbohydrate metabolism is not yet properly understood. The present investigation is an attempt to elucidate the involvement of α and β receptors in carbohydrate metabolism in the above condition. Pigeons were exposed to hot, and cold for 2 hours. Hyperglycaemia developed in both the cases which was further potentiated by the administration of exogenous adrenaline alone and pretreated with reserpine. This effect was blocked by phentolamine. Lactacidemia also developed in both the cases. This effect was blocked completely by propanolol but phentolamine failed to do so. Further investigation with regard to the tissue glycogen level is in progress. The result will be discussed.
34. Adrenoceptor in Dog's Splenic Capsule

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Isoprenaline, beta receptor agonist in the smallest dose range, produced a consistent potentiation of various spasmogens on isolated strip of dog's spleen. This potentiation was completely antagonised by very low concentrations of specific β₁ adrenoceptor blocking agent practolol. Further, in very high doses, isoprenaline per se. produced a contractile response in isolated strip of dog’s spleen. The contractile response to isoprenaline was dose dependent. This effect of isoprenaline was also abolished by beta adrenoceptor blocking agents-practolol and propranolol. Similarly the dose response curve to isoprenaline was shifted to the right in the presence of practolol. Similar results were observed in the dog's spleen in situ. The results in vivo and in vitro studies indicate the presence of beta excitatory adrenoceptors in the splenic capsule of dog.

35. Some Pharmacological Effects of Newly Synthesised Phenylethylamine Analogues

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Present work entails few pharmacological studies with two newly synthesised compounds named SR₂ & SR₃ which are structural variants of SBS-1 (a phenylethylamine analogue). The compound SR-2 produced a triphasic effect on blood pressure viii transient rise followed by a fall and persistent rise, and contraction of spleen and nictitating membrane in doses of 1, 2 and 4 mg/kg (i.v.) whereas SR-3 failed to produce any response in these doses. The mechanism of these responses will be discussed. The compound SBS-1 and SR-2 produced significant dose dependent contractions on rectus abdominis muscle in doses of 20, 40 and 80 μg/ml whereas SR-2 failed to show any effect in these doses. Cumulative dose response curve was construed with SBS-1 and SR-2 and compared with acetylcholine. Although SBS-1 was found to be much less potent (100 times) but was efficacious than acetylcholine. Whereas SR-2 had markedly low affinity as well as efficacy as compared to acetylcholine and SBS-1. d-Tubocurarine in doses which bloked acetylcholine response competitively, blocked noncompetitively the response of both the drugs. Physostigmine potentiation of SBS-1 and SR-2 was much less than that of acetylcholine. It is proposed that these newly synthesised compounds may have a place in neuromuscular disorders.
36. Antiparkinson Property of \( C_{10} \)-Dichol

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\( C_{10} \)-Dichol, an agent which has been reported to inhibit the synthesis of acetylcholine was investigated for its anti-Parkinson effects. \( C_{10} \)-Dichol afforded protection from physostigmine induced death in mice and prevented oxotremorine induced tremor. In nonparalysing doses \( C_{10} \)-Dichol antagonised the neuromuscular blocking properties of nicotine and oxotremorine in a dose dependent manner in the isolated rat phrenic nerve diaphragm preparations. It also prevented the reversal of d-tubocurarine blockade by physostigmine in the rat diaphragm preparation. The effect of \( C_{10} \)-Dichol on the central effects of oxotremorine was also investigated. As \( C_{10} \)-Dichol failed to antagonise the bradycardiac and vasodepressive effects of oxotremorine in rats, it is suggested that \( C_{10} \)-Dichol’s and Parkinson property may be brought about by its action at the skeletal myoneural apparatus.

37. Effect of Atropine Derivatives on Sumithion Induced Paralysis in Dogs

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Dogs of either sex were anaesthetised and respiration was recorded. Twitch responses of tibialis anterior muscles both of limbs to simultaneous repeated stimulation of common peroneal nerves were recorded. Sumithion (Tik--20) was administered intravenously and its effects were observed on respiration and muscle contractions. Effects of atropine sulphate administered intravenously before and after sumithion were noted. The observations will be discussed.

38. Interaction of Oxotramorine and Drugs Inhibiting Transmitter Release at Skeletal Neuro-muscular Junction

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There are numerous evidences indicating various sites viz different areas of brain, spina1 cord and peripheral regulating mechanism as loci of action of oxotremorine, a typical parkinsonimimetic drug, which is a potent muscarinic agent. Oxotremorine has been reported to cause depolarising type of blockade at
skeletal neuromuscular junction. There are numbers of experimental observations which suggest an indirect mechanism of action of oxotremorine at skeletal neuromuscular junction. Employing isolated phrenic nerve-diaphragm preparation, interaction of oxotremorine and morphine, 2-PAM as well as lead acetate, which are reported to cause inhibition of release of acetylcholine at skeletal myoneural junction, were studied. The effects of these drugs were also studied on oxotremorine induced tremor responses in experimental animals in an attempt to elucidate the role of skeletal myoneural effect of oxotremorine in tremorogenesis. Results will be discussed.

39. An Evidence for the Presence of Excitatory and Inhibitory \( \beta \)-Adrenoceptors in the Splenic Capsule of Rabbit

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A study of the effect of isoprenaline on the isolated rabbit's spleen revealed two effects of this drug. In low concentrations isoprenaline was without any effect, but potentiated the spasmogenic responses to acetylcholine. In higher concentrations, it itself induced a spasmogenic response on rabbit's spleen. Propranolol, a beta-adrenoceptor blocking agent completely antagonised spasmogenic responses to isoprenaline and the potentiation of acetylcholine responses caused by the presence of isoprenaline. Practolol, \( \beta_1 \) antagonist potentiated the spasmogenic effects of isoprenaline and the log-dose response curve to isoprenaline was shifted to the left in the presence of practolol. This potentiation was observed in the tissue which was previously treated with priscoline (tolazoline). All these observations suggest an existence of both excitatory and inhibitory beta-adrenoceptors in the splenic capsule of rabbit.

40. Potentiation of Prostaglandins-Evoked Contractions in Isolated Uterine Smooth Muscle by \((+)\) Sotelol and Deoxyaotalol: Specificity, Selectivity and Possible Mechanism of Action

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In earlier studies \((+)\) INPEA (N-isopropyl-para-nitro phenylethanolamine) potentiated the prostaglandins evoked contractions of isolated rat and guinea-pig uteri, while \((-)\) INPEA had no such action. Thus hydroxyl group at the beta
carbon atom may be responsible for such action. To test this possibility experiments were performed with stereo isomers of sotalol (which is structurally similar to INPEA) and deoxysotalol (which does not have any beta-hydroxyl group in the side chain). The effect of these drugs on contractions evoked by PGF\textsubscript{2}\textalpha{} and 15methyl PGF\textsubscript{2}\textalpha{} in the isolated nonpregnant rat and rabbit uteri, and in pregnant rat and human uterine strips was studied. The specificity and selectivity of action was tested by studying their effect on the (i) uterine contraction evoked by some other agonists, and (ii) prostaglandins evoked contractions of isolated fundus strip of rat, isolated tracheal chain and ileum of the guinea-pig respectively. (+) Sotalol and deoxysotalol (100-300 \( \mu g/ml \)) had a marked stimulant action on the uterus. In smaller concentration (10\( \mu g/ml \)), the contractions evoked by prostaglandins were markedly potentiated. Deoxysotalol was more potent than (+) sotalol, 1 B-methyl PGF\textsubscript{a} was potentiated more than PGF\textsubscript{2}\textalpha{}. This suggested that the presence of beta hydroxyl group is responsible for steric hindrance. The potentiation of uterine contraction evoked by prostaglandins was specific and selective. These drugs have a promising therapeutic potential in medical examination of pregnancy, if their selective potentiating effect is confirmed in ‘in vivo’ studies in animals. The combined use of (+) sotalol or deoxysotalol and a smaller dose of prostaglandins may result in a marked reduction in their severe systemic side-effects. Further work is in progress.

41 Adrenergic Neurone Blocking Activity of “Stephania Hernandifolia”
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The plant has been found to contain strong base and weak base. The strong base (SB) fraction of the alcoholic extract was used for pharmacological studies. SB in the doses of 1-2 mg/100 G produced constriction while in doses of 4-6 mg/100 G produced dilatation of the perfused bloodvessels of frog. In smaller doses it did not affect DMPP (50 \( \mu g/100 \) G) responses while in higher doses DMPP was modified. But it always potentiated the vasoconstrictor action of adrenaline (AD 2.5 \( \mu g/100 \) G) without affecting that of acetyl choline (ACh 10 \( \mu g/100 \) G) and barium chloride (BA 10 mg/100 G). These preliminary results suggested that the drug was having either an adrenergic neurone blocking activity or a ganglion blocking action. In the present communication the results with experiments aimed at the evaluation of adrenergic neurone blocking activity have been included. In isolated vas deferens of rat, SB in the concentrations of 5-10 \( \mu g/ml \) inhibited the responses to electrical stimulations but potentiated the responses of noradrenaline (NA 1-2 \( \mu g/ml \)). It also inhibited the relaxant effect
of sympathetic stimulation of ileum in Finkleman preparation without affecting the AD responses. SB blocked the positive chrono- and inotropic effects of sympathetic stimulation in atropinised isolated innervated frog auricles, while the effects of NA and AD were unaffected. Similarly SB blocked the vasoconstriction after electrical stimulation of rabbit’s isolated central ear artery segment without affecting the NA & AD. The results suggest that the SB has adrenergic neurone blocking activity like that of guanethidine.

42. **Effect of Some Biogenic Amines on the isolated Human Vas Deferens**  
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Effects of some biogenic amines were studied on human vas deferens to gain an insight into the physiological control of this organ in humans. The specimens of vas deferens (6 to 7 mm) obtained from vasectomy operations showed no spontaneous activity when suspended in isolated organ bath containing Kreb’s Hensleit solution maintained at 37°C. Adrenaline and noradrenaline stimulated the tissue by inducing rhythmicity in these quiescent tissues. Dose-dependent increase was observed in all the three parameters of rhythmic contractions, viz. peak tension, frequency and total tension with both of these drugs. These responses were competitively blocked by DHE. Adrenaline was found to be 5 times more potent than noradrenaline and the maximum frequency achieved with adrenaline was significantly more (P<0.05) than that obtained with noradrenaline. Isoprenaline and histamine in comparatively high doses also produced rhythmic contractions of vas deferens but marked tachyphylaxis was observed with both of them. Acetylcholine and 5-hydroxytryptamine were unable to produce any activity even at high concentrations. The study indicates a primary role of adrenaline in the initiation and maintenance of pulsatile contractions of human vas deferens during ejaculation. Also the results demonstrated that human vas deferens contains exclusively alpha-adrenoceptors.
43. Brain Catecholamines in Clinical Hypertension

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Recent evidences suggest that central catecholamines (CA) are involved in the regulation of blood pressure. Changes in central CA have also been observed in experimental hypertension in animals. However, studies are not available to substantiate the role of CA in the clinical hypertension. In the present study estimation of CSF 3-methoxy-4-hydroxy phenyl glycol (MHPG), a selective metabolite of CA in the brain was done in normal and hypertensive individuals with a view to ascertain the significance of central CA in the pathogenesis of hypertension. Twenty cases of systemic hypertension of varied etiology and 8 matched controls were included in the present study. There was statistically highly significant increase in CSF, MHPG values in hypertension and this was directly related to the severity of the disease. Significant fall in CSF MHPG occurred following therapy with alpha methly dopa and clonidine.

44. Importance of Spinal Autonomic Loci in Arrhythmia Following Coronary Ligation

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Coronary artery ligation performed in two stages consistently produced ventricular ectopics associated with raised plasma catecholamine (PC) and free fatty acid (FFA) levels in dogs. Ether or pentobarbitone anaesthesia completely blocked the cardiac irregularities and lowered the PC and FFA. On the other hand, chloralose anaesthesia did not influence the ventricular ectopics, PC and FFA. Haemorrhagic hypotension also did not affect the ventricular ectopics following coronary artery ligation. Various neural factors concerned in the genesis of
cardiac arrhythmias following coronary artery ligation were studied by pharmaco-
logical and surgical techniques, in chloralose anaesthetized dogs. Bilateral
vagotomy, mid-collicular or spinal (C1) transection did not significantly affect the
ventricular ectopics. Spinal cord (C1-T4) destruction completely blocked
ventricular ectopics, restored normal rhythm and lowered PC and FFA levels.
Spinal anaesthesia with xylocaine also completely abolished ventricular ectopics.
Cardiac sympathectomy or bilateral adrenalectomy significantly inhibited the
ventricular ectopics and lowered PC and FFA. Ganglionic blockade, adrenergic
neuron blockade of \( \beta \)-adrenoceptor blockade restored the normal sinus rhythm.
These results demonstrate the importance of spinal autonomic loci in the integra-
tion of reflex cardiac arrhythmia arising from myocardial ischaemia.

45. Evidence Supporting the Contention that Hypotensive Response
to alpha Methyldopa is Centrally Mediated

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Various mechanisms of antihypertensive action of alpha methyldopa (AMD) have
been proposed. The one widely held view is that the drug may be converted to
secondary metabolites which in turn produce the hypotensive effect. Consider-
able controversy exists whether this action is exerted peripherally or centrally. In
the present study which was conducted on anaesthetised dog and cat. an attempt
has been made to investigate the relative role of peripheral and/or central
components of action in the hypotensive effect of AMD. Two sets of experiments
were performed. In the first set, AMD was administered intravenously (IV)
to a group of dogs and when a maximum fall in blood pressure (BP) appeared,
it was followed by a second dose given intracerebroventricularly (ICV). In the
second set the order of IV and ICV doses was reversed. It was observed
that the fall in BP caused by an IV dose of AMD was further enhanced
by a subsequent ICV dose. However, an IV dose of AMD given after ICV
injection, did not modify the hypotensive effect of the latter. Administration of
phentolamine by ICV route, blocked the hypotensive response to IV as well as
ICV injection of AMD. Similarly no hypotension was observed after AMD in
animals in which spinal section (C1) was done. In DDC pretreated animals, the
hypotensive response to both IV and ICV dose of AMD was not observed. The
results of the present investigation suggested that in producing the hypotensive
response AMD. central conversion to its metabolites plays a role than that in
periphery and probably it is the central component of action which owes the
effect even when the drug is administered peripherally. Further, it seems that the
conversion of AMD to alpha methyldopamine does not contribute at all in the
hypotensive response to AMD.
46. Antiarrhythmic Activity of Metoprolol-A New Cardioselective Adrenergic Receptor Antagonist

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The antiarrhythmic activity of metoprolol (H 93/36=(±)-1-isopropylamino -3-(p-2 (2-methoxyethyl)-phenoxy)-2-propanol) has been studied on (a) adrenaline induced cardiac arrhythmias in cats (b) ventricular arrhythmias produced by occlusion of anterior descending branch of left coronary artery in mongrel dogs (c) Ouabain induced ventricular fibrillation in guinea-pigs. Metaprolol possesses membrane stabilising activity apart from its beta blocking activity. In this respect it resembles propranolol. However, the advantage of metaprolol over propranolol is that it is cardioselective as well. The result obtained was compared with that of propranolol. Both propranolol and metoprolol were found to have a dose dependent, significant antiarrhythmic activity in all the three models of arrhythmia. Propranolol (0.5 mg/kg), metaprolol (2.5 mg/kg) protected the animals against adrenaline induced cardiac irregularities. The incidence of ventricular arrhythmia in the conscious coronary-ligated dogs was markedly reduced by 3 mg/kg of propranolol and metaprolol. Propranolol and metaprolol were also effective in protecting the animals against ouabain induced cardiotoxicity in the dose level of 2 mg/kg and 15 mg/kg respectively. The significance of these results will be discussed in the light the wide spectrum of experimental antiarrhythmic activity of metaprolol coupled with its cardioselectivity.

47. Nature of Histamine Sensitive Receptors in the Rat Heart

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Histamine and several natural products containing histamine were tested on the isolated heart preparations of guinea pigs and rats in order to compare the relative sensitivities of the two species to histamine. While histamine and the natural products rich in histamine content show the usual expected effects on the guinea pig heart, these agents failed to show a dose-dependent positive inotropic or chronotropic effects on the rat heart. From the data obtained in the present study it appears that histamine sensitive receptors in the usual sense of cardiac reactivity to histamine are either absent in the rat myocardium, or if present may be inhibitory in nature. The coronary vessels of the rat heart on the other hand appear to be devoid of either excitatory or inhibitory histamine receptors.
48. A New Centrally Acting Hypotensive Agent

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Successful use of clonidine, an imidazoline derivative, in the treatment of hypertension has generated great interest in centrally acting hypotensive agents. In the present study several substituted piperazino-imidazolines synthesized in our department were evaluated for central hypotensive activity. Only phenyl piperazino imidazoline (PPI) induced a sustained and dose-dependent hypotension and bradycardia. Other compounds either elicited a mild hypotensive activity of short duration or induced a vasopressor response. Further studies showed that PPI on intravenous administration blocks bilateral carotid occlusion responses without affecting pressor responses induced by preganglionic stimulation of the splanchnic nerve and intravenous administration of noradrenaline. PPI did not inhibit the responses of the nictitating membrane induced by pre-ganglionic stimulation of fibres of cervical vagosympathetic trunk. These observations rule out any significant effect of the compound on the adrenergic neurons and sympathetic ganglia. One tenth of the intravenous dose of PPI when administered intracerebroventricularly produced the same degree of fall in blood pressure which was associated with marked bradycardia and blockade of carotid occlusion responses. Noradrenaline (i.v.) induced pressor responses were unaltered. Qualitatively similar effects were obtained with intravertebral injection of PPI. These results demonstrate that PPI is a central hypotensive agent with low acute toxicity (LD 500 mg/kg i.p.).

49. Antagonism of Clonidine Hypotension By Intracisternal 5, 6-Dihydroxytryptamine Pretreatment in Rabbits

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Clonidine, an imidazoline derivative, induces hypotension in a number of species. The hypotensive action of clonidine has been shown to be due to stimulation of a-adrenoceptors in cardiovascular ‘centres’. However, presence of 5-hydroxytryptamine (5-HT) containing neurons has been shown in different areas in the central nervous system including brain-stem reticular formation. Therefore, the present study was carried out to investigate the hypotensive effect of clonidine in rabbits pretreated with intracisternal injection of 5, 6-dihydroxytryptamine (5,6-DHT) which produces selective lesion of 5-HT containing neurons. Clonidine
(30μg/kg, i.v.) was found to induce hypotension in control animals. In animals pretreated with intracisternal 5, 6-DHT the hypotensive response of clonidine was blocked. This was associated with significant reduction of 5-HT in midbrain, medulla-pons and spinal cord. The significance of these observations will be discussed.

50. Hypotensive Activity of Some Newer Piperazino Quinazolones
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Several piperazines and quinazolones have been shown to possess antihypertensive activity. In the present study, therefore, we have evaluated seventeen piperazino quinazolones synthesized in our department for possible hypotensive activity in anaesthetized dogs. In this series several compounds induced fall in blood pressure. Three compounds (Cl, Q18 and Q20) induced potent hypotensive activity of approximately 60 min duration. These agents exhibited bradycardia during first few minutes of their effect and blocked the carotid occlusion (CO) responses. The pressor responses induced by noradrenaline injection or splanchnic nerve stimulation were either unaffected or were partially inhibited different compounds. These results show that some of the piperazino quinazolones possess potent hypotensive activity and deserve further study.

51. Central Cardiovascular Effects of Nicotine
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Intracerebroventricular injection of nicotine has been shown to produce variable effects by different workers. In pentobarbitone (30 mg/kg i.p.) anaesthetized cats nicotine (250 μg/ml) superfusion into posterior hypothalamus produced hypertension and tachycardia. This response could be blocked by a nicotinic blocker chlorisoneamine as well as a β-adrenergic blocker, sotalol. In medullary reticular pressor area, however, nicotine superfusion induced a biphasic response consisting of an initial rise in blood pressure with tachycardia followed by hypotension and bradycardia. The pressor and tachycardia phase were successfully abolished by chlorisondamine, whereas the depressor response and bradycardia were blocked by an α-adrenoceptor blocking agent, piperoxan as well by 6-hydroxy-dopamine pretreatment. It may therefore be concluded that in posterior hypothalamus nicotine by stimulation of nicorinic cholinergic receptors induces
hypertension and tachycardia which are attributed to central catecholamine release. On the contrary, in the medullary pressor area it produces an excitatory cardiovascular response by stimulation of nicotinic cholinoreceptors whereas the release of catecholamine by nicotine in this area evokes inhibitory response.

### 52. Role of Vascular Reactivity in the Development of Spontaneously Hypertensive Rats

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Hyper-reactivity of blood vessels to different vasoconstrictor agents has been extensively studied in different types of hypertension. The mechanism for this hyper-responsiveness and its role in the development of hypertension is not clear. In our laboratory we have succeeded in isolating rats from an inbred colony of spontaneously hypertensive rats, differing in their blood pressure and which are classified as hypertensive (SH) and normotensive (NSH). These rats were used for investigating the relationship between blood pressure levels and vascular reactivity to noradrenaline (NA) and angiotensin II (ANG) in vascularly isolated but neurologically intact hindquarter and mesenteric artery preparations. The vascular reactivity to NA and ANG has been found to be similar in SH and NSH rats. In perfused mesenteric artery preparation from NSH rats, the dose response curves produced by NA exhibited similar steeper slopes and increased maximal response as compared to SH rats. These results suggest that increased vascular reactivity of blood vessels is independent of the development or maintenance of elevated blood pressure.

### 53. Reversal of Digoxin Induced Cardiac Arrhythmias by Nickel chloride

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The divalent metal ions show a variety of pharmacological actions. They are known to stimulate and depress a variety of enzyme systems of heart, liver, kidney etc. and some of them produce a profound change in the carbohydrate metabolism. The preliminary observations that Ni^{2+} effectively antagonised some of the toxic effects of digitalis on amphibian heart lead us to study in the mammalian species. The experiments were done in dogs anaesthetised with pento-barbitone sodium and digoxin given intravenously in a dose of 150μg/kg which induced supraventricular arrhythmias. This was successfully counter-
acted by 1 mg/kg of NiCl₂ while NiCl₂ at that dose did not produce any cardiovascular changes. Isolated hearts of rabbits, guineapigs and rats were perfused with increasing doses of digoxin (about 300 µg) along with physiological salt solution till tachycardia followed by cardiac arrest. In such hearts NiCl₂ (about 3 mg) reinitiated contractions and normal rhythm was restored within 2-3 minutes. The EKG changes of a supraventricular arrhythmia (lead II) completely disappeared. Sinus rhythm was restored and the cardiovascular status of the animal (which was digitoxic) eventually returned to normal. On the contrary, in dogs not treated with NiCl₂ a progressive worsening of the cardiovascular system resulted in the death of the animal. Ni²⁺ is reported to compete with Ca²⁺ at cell membrane sites for the ingress into the cell and thus inhibit the calcium current and modify the action potential.

54. Effect of Sympathomimetic Amines and Monoamine Oxidase Inhibitors on the Blood Pressure of Dogs

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The effects of adrenaline, noradrenaline and ephedrine were studied on the blood pressure of twenty normal anaesthetised dogs before and after the administration of the monoamine oxidase inhibitors tranylcypromine, pargyline, nialmide and isocarboxazide. The effect of adrenaline and noradrenaline on blood pressure were not potentiated by these MAO inhibitors, while those of ephedrine were significantly augmented by them. The results and conclusions shall be discussed.

55. Effect of L-Dopa on the Blood Pressure of Anesthetised Animals

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Intravenous injection as well as oral administration of L-dopa has been reported to produce hypertension. The observation that L-dopa produces orthostatic hypotension is also well documented. The mechanism by which L-dopa produces the cardiovascular response is of great theoretical interest but not yet been fully established. An attempt has been made to study the effect of L-dopa on blood pressure after intravenous administration in anesthetised animals. The results and their significance will be discussed.
A controlled clinical trial of rifampicin plus ethambutol has been compared with the standard regimen of ethambutol plus pyrazinamide plus cycloserine in the management of salvage cases of pulmonary tuberculosis, in whom the standard chemotherapy has failed. The results at one year have been presented. All patients were adults with sputum positive pulmonary tuberculosis with INH resistance, who had been previously treated with standard antitubercular drugs but not with the drugs under study. They were allocated to the following regimens at random. 1. Ethambutol plus rifampicin daily (R+Et). 2. Ethambutol plus rifampicin biweekly (R+Et). 3. Ethambutol plus rifampicin daily for six months followed by twice weekly (REt+REt). 4. Ethionamide plus pyrazinamide plus cycloserine daily (E+Pz+C) for six months followed by ethionamide plus pyrazinamide daily (E(Pz}) as standard control regimen. The radiographic improvement and monthly sputum culture results were similar in all the regimens. At 12 months 85% of REt, 79% of REt, 89% REt+REt, and 80% of Et+Pz+C, patients had a favourable response. In some, adverse reactions to ethambutol or rifampicin were encountered. Mainly the adverse reactions to rifampicin were cutaneous or increase in transaminase levels without jaundice. Respiratory syndromes were commonest, but it was less common in daily regimen as compared to biweekly regimen. Only 3% patients on intermittent regimen had to discontinue the drugs. Episode of acute renal failure was observed in one patient in the present study. Other adverse reactions eg. shortness of breath, asthma-like symptoms. jaundice end purpura, although uncommon, are clinically important and should be managed with caution. Adverse reactions on the standard reserve regimen were not infrequent and led to termination of drug/drugs in some cases; the important ones being neuro-psychiatric reactions. When the therapeutic efficacy, the management of adverse reactions and the cost-effectiveness are taken into account, biweekly rifampicin plus ethambutol regimen emerged to be the regimen of choice for the out-patient treatment,
57. Trial of Some Chemotherapeutic Agents in Equine Babesiosis
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Chemotherapeutic trials on splenectomized donkeys, experimentally infected with *Babesia equi* were carried out with berenil, berenil plus reverin and babesan. Berenil (6 mg/kg, i.m.) or the combination of berenil (6 mg/kg, i.m.) plus reverin (10 mg/kg i.m.), when given in early stage of infection were found effective in causing the clinical recovery, though the recovery rate was slow. Babesan was found ineffective when given even in the early stage of infection and this drug was irritant. However, on the basis of clinical recovery, survival of the animal, suppression of parasitaemia, improvement of the haematological losses and the cost of treatment, berenil alone was considered as the drug of choice.

58. Effect of Chloramphenicol and Clotrimoxazole on ADP Induced Platelet Aggregation and Some Other Related Parameters
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Chloramphenicol, is an antibiotic commonly employed in clinical practice and is known to cause blood dyscrasias. Another antibacterial agent introduced recently and used widely is clotrimoxazole. We thought, it interesting to know whether similar effects on hemopoietic system are encountered with this agent. The present study was therefore undertaken to evaluate the effects of these two antibacterial agents in various doses on platelet aggregation and related parameters. Results will be discussed.

58. Antiflarial Activity of Livamisole Using Setaria Cervi as Test Organism
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Adult *S. cervi* and its nerve-muscle preparation inhibits spontaneous rhythmic movements when suspended in an isolated organ bath containing modified ringer's solution. Addition of levamisole (2.5 μg/ml) to the bath fluid caused immediate increase in the tone as well as the rate of movements. The amplitude
ABSTRACTS

was reduced. After about 5 minutes the amplitude of contractions started decreasing. Recovery to the original rate and amplitude was obtained after about 10 minutes. Recovery in tone started after about 45 minutes and was normal after about 90 minutes. Higher concentration (25 $\mu$g/ml) caused a biphasic response characterised by initial stimulation followed by paralysis. The effect on nerve muscle preparation was similar in nature to that observed with the whole worm. However the concentration required to produce an equivalent effect in the nerve-muscle preparation was $1/5$th of that required with the whole worm. In rats implanted intra-peritoneally with 2 male and 2 female adult worms levamisole caused complete eradication of microfilariae from peripheral circulation of 7 of the 8 rats in a dose of 5 x 25 mg/kg and in all the rats with a dose of 5 X50 mg/kg. Lower doses were, however, ineffective. The effect of levamisole was short lived and microfilariae reappeared in peripheral circulation. The microfilaricidal action was significant only in a dose of 5 x 50 mg/kg/day.

60 Observations on the Adverse Reactions to Regimens for the Treatment of Pulmonary Tuberculosis
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In the controlled trial in Varanasi among Indian patients with pulmonary tuberculosis, in whom the treatment with standard regimens had failed, were allocated at random to the following regimens of chemotherapy: (1) Rifampicin plus ethambutol daily (R+E). (2) Rifampicin plus ethambutol twice weekly (REt). (3) Rifampicin plus ethambutol daily for six months followed by twice a week (REt+REt) rifampicin and ethambutol. (4) Ethionamide plus pyrazinamide Plus cycloserine daily for six months (E+Pz+C), followed by ethionamide plus pyrazinamide daily (E+Pz), as standard control regimen. In daily rifampicin regimen, the dose of rifampicin was 600 mg a day for all the patients. In the intermittent regimen the dose of rifampicin was 900 or 1200 mg according to the body weight. In the daily regimen the dose of ethambutol was 25 mg/kg body weight and in twice weekly regimen it was 35 mg/kg body wt. Answers to a questionnaire on allergic reactions, the results of prick tests with standard allergens, and size of tuberculin reactions during the chemotherapy showed no association with the occurrence of adverse reaction to daily or intermittent rifampicin group. Mantoux test during the chemotherapy provided no evidence of an immunosuppressive effect of rifampicin. Mean platelet counts at 12 months were significantly lower than those at 3 months. On the twice weekly regimen and in the control regimen it was within normal limits. The adverse reactions in patients on intermittent rifampicin regimen were cutaneous, abdominal, respiratory and
haematological. In addition, abnormal liver function tests were also encountered. There was an association of adverse reactions between the interval and the dose of rifampicin and in our group highest incidence was noted in high dose twice weekly rifampicin. Adverse reactions on standard regimen were sometimes serious where it became necessary to discontinue the drug.

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**CLINICAL PHARMACOLOGY**

61. Adrenergic and Cholinergic Interactions of Mianserin and Amitriptyline

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Mianserin a new tetracyclic compound has been recently found to possess antidepressive activity similar to amitriptyline in several double-blind studies. The clinical pharmacology of mianserin was studied in patients suffering from primary depressive illness (during steady state plasma concentration of the drug) and compared to that of amitriptyline in a double-blind study. Although the antidepressive activity of the two drugs are almost identical, mianserin appears to be free of anticholinergic effects and has no peripheral adrenergic interactions. The anticholinergic effects were measured by the change in the salivary volume, pupil diameter and interactions with guanethidine and thymoxamine on the pupil. The peripheral adrenergic interactions were studied by determining tyramine-dose/pressor response test, noradrenaline-dose/pressor response test and the interactions of tyramine and hydroxyamphetamine in the iris. The implications of these findings for the validity of biogenic amine hypothesis of depression will be discussed.
82. The Effect of Change in Acid Base Balance on Absorption and Elimination Kinetics of Sulphonamides

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Controlled clinical trial was conducted on six healthy male volunteers. The effect of change in acid base balance on absorption and elimination kinetics of sulphonamides with different protein binding capacity was studied. Each volunteer was subjected to following six treatments according to the latin square design:

1. Sulphamethizole (500 mg) and NaHCO₃
2. Sulphamethizole (500 mg) and NH₄Cl
3. Sulphasomidine (500 mg) and NaHCO₃
4. Sulphasomidine (500 mg) and NH₄Cl
5. Sulphamethoxypyridazine (500 mg) and NaHCO₃
6. Sulphamethoxypyridazine (500 mg) and NH₄Cl

Sulphonamide concentration in serum and urine was determined colorimetrically. Results were analysed and will be discussed.

63. Microsomal Metabolism of Antipyrine in Malnutrition

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Literature is replete with evidences that nutritional deficiencies can alter drug metabolism in experimental animals. However, studies evaluating the capacity of malnourished subjects to metabolise drugs are scanty. An investigation was therefore undertaken to evaluate microsomal enzymes in human subjects using antipyrine half life as an index of drug metabolism. In addition, plasma gamma glutamyl transpeptidase activity (Y-GT) was determined not only to evaluate liver damage, but also to determine the extent of enzyme induction after phenobarbitone administration. Four groups of subjects/patients were chosen for the investigation. Group 1 consisted of normal male healthy adult volunteers free from smoking habits, Group II consisted of normal male healthy adults with smoking habits, Group III consisted of undernourished apparently normal male patients and Group IV was formed by patients with nutritional oedema—a severe manifestation of protein-calorie malnutrition. Serial blood collection were made at regular intervals after antipyrine administration and pharmacokinetic data were calculated. In a limited number of subjects antipyrine half life and Y-GT activity were determined both before and after phenobarbitone administration. Serum albumin was estimated in all. The results of the study indicated that the microsomal enzyme activity in smokers and undernourished subjects was in an induced state, thus shortening the antipyrine half life. On the other hand in patients with nutritional oedema, the antipyrine half life was prolonged and also...
γ-GT was elevated suggesting a liver damage. However, the induction after phenobarbitone administration was similar in all the groups. Clinical implications will be discussed.

64. Antibiotic Drug Surveillance

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A surveillance was conducted to assess the comparative use of antibiotics in 2 general surgical wards with a view to finding out the pattern of prescription of antibiotics and how the use of these antibiotics influenced the stay of the patients in the hospital. The total number of patients involved was 137 and 160 in the two units respectively. The commonest operations performed were hydrocele and hernia. The commonest antibiotic used was penicillin combined with streptomycin. Next in order was procaine penicillin. Other antibiotics were also used, though less frequently. Duration of patient’s stay in the hospital did not show any significant difference between the two groups. There was also no difference in the extent of use of antibiotic in these two groups. Implications of such a study and its limitations in hospital environment will be discussed.

65. Interactions of Five Psychosedative Drugs in Acute Ischaemic Heart Disease

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The interactions between pethidine, heparin and phenindione on one hand with 5 psychosedative drugs-chlorpromazine, chlordiazepoxide, haloperidol, meprobamate, and methaqualone on the other were studied in proved cases of acute ischaemic heart disease. Six groups of 10 patients each received pethidine, heparine and phenindione. Five groups received respective psychosedative drugs for three days, in addition to the above drugs. The sixth control group received placebo in addition to pethidine, heparine and phenindione. Chlorpromazine prolonged prothrombin, bleeding and clotting times. This may be due to the decreased platelet adhesiveness and aggregation and increased hypoprothrombinemic effects. Meprobamate produced an opposite effect which could be due to hepatic microsomal enzyme induction. Haloperidol raised the bleeding and clotting times significantly to almost double the control values. The study indicates that phenindione dosage needs to be adjusted in patients, who also receive either chlorpromazine, meprobamate or haloperidol.
66. Clinical Study of a New Diuretic HOE 118

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Controlled clinical trial conducted on six male volunteers satisfying the criteria of health. The object was to test the efficacy of a new diuretic HOE 118 given with and without aldactone against that of a standard diuretic and placebo. Each volunteer for this purpose was subjected to the following six treatments administered according to the latin square design: (1) Lasix-40 mg. (2) HOE 118-3 mg. (3) Placebo. (4) Lasix-40 mg+aldactone-25 mg. (5) Hoe 118-3mg +Aldactone-25 mg. (6) Placebo+aldactone-25 mg. The parameters studied were urinary pH, Na/K ratio and total volume of excretion. Results were analysed and will be discussed.

67. Influence of Dimethicone on Sulphadiazine Absorption

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Dimethicone is often employed for flatulence, a common gastrointestinal symptom in this country. The effect of prior dimethicone administration on sulphadiazine absorption in man was investigated in course of the present experiments. Following administration of sulphadiazine orally to healthy persons, in whom gastrointestinal lesions had been excluded, plasma sulphadiazine levels were estimated at predetermined times. Commencing three days later, dimethicone (40 mg, t. i. d., orally) was administered for 5 days. 1½ hours after the last dose, sulphadiazine again administered and plasma levels estimated. It was found that following dimethicone, orally administered sulphadiazine led to lower peaks of plasma sulphadiazine level, and absorption rate constant was lowered. Area under curve also decreased. Prior administration therefore appears to reduce the bioavailability of sulphadiazine.

68. Cardiac Effects of Paracetamol

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The widely used antipyretic analgesic, paracetamol, though, claimed to be practically non-toxic, yet recent studies suggested that the drug is potentially
toxic. Paracetamol in therapeutic doses is devoid of cardiotoxicity in non-cardiac patients. However, myocardial damage with toxic doses (poisoning) of paracetamol have been reported. The present study was undertaken in healthy adult male volunteers to examine if paracetamol in doses within therapeutic range could produce any cardiac effect. Ten healthy adult male volunteers were studied by double blind cross-over test using oral paracetamol (crocin) and aluminium hydroxide (Aludrox) tablets. Pulse rate and blood pressure were recorded before and after (1 hr) drug administration. Significant bradycardia was observed in paracetamol treated volunteers. Further studies were undertaken in mongrel dogs to elucidate the mechanism of bradycardia. The results will be discussed.

69. Topical Corticosteroid and Skin Infection

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Spreading bacterial and fungal infections are known to occur more frequently under systemic corticosteroid therapy. This is, however, controversy as to the effect of local corticosteroid therapy in them. Present paper aims at discussing the controversial issues on use of corticosteroids locally, on superficial bacterial and superficial fungal infections of skin. Data have been recorded from the experimental work on human volunteers, assessing the progress primarily on clinical observations made by paired comparison. Healthy skin of human volunteers was used to study the effects of topical corticosteroids on experimental skin infection with *staphylococcus aureus*, where as controlled study on two sides on experimental fungal infection were undertaken and followed up for a considerable length of time (4-6 weeks). Observations demonstrated that corticosteroids when applied topically, do not stimulate growth of either *staphylococcus aureus* or superficial fungal infections (*T. rubrum* was experimental strain for fungal infection study).
70. Effects of Phenobarbital, Ethanol and 2-[2-(3-Pyridy) vinyl]-3-0-Tolyl-3, 4-Dihydroquinazolin-4-One (SRC 909) on the Reproductive Processes of Female Albino Rats

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Chronic feeding of phenobarbital, ethanol, and SRC 909 for 15 days prior to mating in fertile female albino rats showed decrease in litter size and increase in the mortality rate of the pups. Even though the birth rates of the pups were within the normal range, the subsequent growth rate (recorded upto 28 days) was slower when compared to the control.

71. Spermicidal Activity of Some Naturally Occurring Saponins

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The recent report that certain saponins have spermicidal properties prompted us to investigate other saponins obtained from plants of different botanical families. In the present study, the saponins were isolated from the seeds of Albizzia-procera (A) and Pithecolobium dulce (B) (both Leguminosae) and fruit pulps of Belanitis roxburghii (Zygophyllaceae) (C) and Blighia sapida (Sapindaceae) (D) Barring the saponin obtained from B. roxburghii the aglycone of others belong to oleanane series of triterpenoids. The saponin powders were taken in soerenson's isotonic phosphate buffer (pH 8.0) containing 1.7% glucose and 0.38% NaCl for maintaining good sperm motility. Out of the four saponins, the saponin obtained from B. sapida (D) showed 100% spermicidal activity. Concentration as low as 0.05% caused instantaneous immobilization of human spermatozoa. The saponin obtained from Pithecolobium dulce was next in order. However, the other two remainings were found to be inactive. These saponins also showed antibacterial activity which may have added advantage. These saponins seem to hold a promising clinical potential and need further exploration.
72. **Hypoglycemic Effect of Manganese Chloride**

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Manganese chloride elicited hypoglycemic effect in the normal rats and dogs. This effect persisted for 4 to 6 hours. However, manganese chloride failed to produce hypoglycemic effect in alloxan induced diabetes in rats. The glucose tolerance curve (G.T.C.) pattern both by I. V. and oral glucose administration was different in normal and manganese chloride treated rats. G. T. C. pattern did not alter on pretreatment with manganese chloride in alloxan induced diabetic rats. The results indicate that manganese chloride elicits hypoglycemic effect only when insulin is present possibly by enhancing insulin release.

73. **Effect of Raised Temperature on Antidiuretic Hormone (ADH) Levels of Posterior Pituitary**

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We reported earlier that increased body temperature to 40°C causes decrease in glomerular filtration rate thereby reducing the urine volume. It was considered pertinent to study role of ADA during pyrexial periods in rats and children. Study was made in 15 charles foster rats, and 6 pyrexial children. Experimental design in rats was similar as reported by us earlier. Pituitary ADH was extracted and serum proteins and haematocrit were determined in capillary centrifuge tubes. Urinary ADH of children were extracted by zinc ferrocyanide absorption method. Pressor activity was estimated in rats by standard method. Results of the study indicate that at body temperature of 37°C pituitary contents of ADH is \(84 \text{ mU/100 gm of body weight}\) whereas when temperature is raised to 40°C total pituitary contents of ADH decreased to \(51 \text{ mU/100 gm of body weight}\). This reduction of 40% is statistically significant \((P<0.05)\). When the body temperature was reduced to 34°C there was, however, no change in pituitary ADH content. Serum proteins and haematocrit did not change significantly. It is, therefore, concluded that reduction in urine flow during the pyrexial phase is not only due to reduction in glomerular rate filtration but also a result of increased of anti-diuretic hormone in plasma due to the depletion of pituitary ADH. In pyrexial children results indicate that mean urinary level of ADH fell from 1.59 \((0.30-4.45) \text{ mU/hr}\) during pyrexia to 1.02 \((0.18-3.60) \text{ mU/hr}\) during apyrexial phase. This difference is statistically significant \((P <0.01)\). So it is concluded that during heat stress the reduction in urinary volume is due to decrease in glomerular filtration rate and increased excretion of ADH both in rats and in human beings.
74. Serum Oxytocinase in Normal Pregnancy
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36 women during different trimesters of normal pregnancy and nonpregnant healthy women were included in this study. 4 ml blood was collected from anti-cubital vein and plasma was separated from heparinized blood. Plasma oxytocinase and serum proteins were measured. Result of the study indicates that serum proteins do not show any change in various trimesters of pregnancy. However, there was significant change in serum oxytocinase levels during pregnancy. In first trimester, it was $0.819 \pm 0.058 \text{mg/100 ml S/hr}$ (p value <0.05) while the normal serum oxytocinase was $0.630 \pm 0.111 \text{mg/100 ml S/hr}$, but this change is not significant if the enzyme is expressed/gm of circulating serum proteins. It is interesting to note that this change as well as change in the serum oxytocinase levels during 2nd and 3rd trimesters are highly significant ($1.408 \pm 0.147 \text{mg/100ml S/hr}$ and $3.850 \pm 0.461 \text{mg/100mlS/hr}$, p value <0.01). Thus it is concluded that serum oxytocinase level is significantly changed during second and third trimesters of normal pregnancy showing increasing secretion of enzyme from trophoblastic cells of placenta.

75. Antioestrogenic and Antiovulatory Activity of Some Newer Substituted Coumarins
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Antioestrogenic, antifertility and anti-implantation activity have been reported in coumarins by several workers. Based on the above observations we have synthesized some newer 7-(4-substituted thiosemicarbazido methoxy)-4-methyl coumarins. These compounds have been evaluated for their antioestrogenic activity against oestradiol induced increased in uterine weight in immature albino rats maintained on standard diet. It was observed that all the seven compounds tested possessed antioestrogenic activity to a varying degree when given in a dose of 80 mg/kg orally. The compounds were further evaluated for antiovulatory activity against copper acetate induced ovulation in adult female non-pregnant oestrogenized rabbits in a dose of 80 mg/kg orally. All the seven compounds blocked ovulation to a varying degree (from 50 to 100%). It was interesting to note that there was a close correlation between antioestrogenic and anti-ovulatory activity. The results will be discussed in the light of positive feed back effect of oestrogen on ovulation. The ALD$_{50}$ of these compounds was found to be between 800 to 1000 mg/kg orally in albino mice.
76. Inter-Relationship Between the Blood Glucose Concentration and the Glucose Concentration Available to Brain

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The possibility of some structure in the brain having a physiological influence on the peripheral blood sugar was suggested earlier on the basis that puncture of the floor of fourth ventricle produced a prolonged hyperglycemia. Though it has been established that the blood sugar level is directly under the influence of pancreas, the C. N. S. has also been implicated in its control from time to time. In the present investigation an attempt has been made to study whether alterations in the glucose level available to the brain influence, in any way, the level of peripheral blood sugar. Dogs and rabbits were used as experimental animals. The experiments were done in dogs anaesthetized with pentobarbitone with a cannula in lateral ventricle and in rabbits by implanting I. C. V. cannula. Blood glucose estimation was done as usual and plasma insulin estimation by using the rat diaphragm method. The possibility of some central structures responding to alterations in the glucose available to them is discussed.

77. Effect of Hormones on the Responses to Catecholamine on Longitudinal and Circular Muscle of Isthmus of Rabbit Fallopian Tube

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Ova are retained at the ampullary-isthmic junction of the rabbit oviduct for about 16 to 18 hours and then take about two additional days to traverse the isthmus. The mechanism which control isthmic ovum transport has not been fully elucidated. Anatomical and physiological studies including the demonstration of alpha and beta adrenergic receptors suggest that the isthmus behaves as an adrenergic sphincter. Specifically it has been postulated that in circular isthmus, beta adrenergic receptors become more active after ovulation. But the exact mechanism is still not clear. It is also not clear whether increase in beta receptor activity occurs in longitudinal muscle of isthmus or not. So in the present study the responses to noradrenaline, adrenaline, oxymetazoline, barium chloride, isoprenaline and aminophylline were studied in different hormonal conditions on both circular and longitudinal muscles of isthmus. The results obtained and their significance will be discussed.
78. An Analysis of the Responses of the Teleostean Fish Intestine to Histamine

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The effects of histamine on the isolated intestines of two teleostean fishes *C. batrachus* and *H. fossilis* have been studied. No difference was found in the nature of the responses to histamine in either fish. Histamine caused either relaxation or contraction or a combination of both. The contractions were blocked by mepyramine and the relaxations by propranolol or DCI. The inhibitory action of histamine seems to be indirect response mediated through the release of catecholamines. Atropine and hexamethonium completely blocked the contractile responses to histamine. The effects indicate the involvement of a cholinergic mechanism in the contractile action of histamine on the intestine of these two fishes.

79. Effect of Propranolol on Mucoproteins and Mucoproteoses of Gastric Juice in Albino Rats

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Earlier studies showed a dose dependent biphasic response of few β-adrenoceptor blocking agents; the small doses increased the acid output while the higher doses decreased the acid output in pylorus ligated rats and in pentagastrin stimulated gastric acid secretion by continuous stomach perfusion method. This increase in acid output was accompanied by an increase in the ulcer index. To study the role of β-adrenoceptor blocker on the mucus factor, the effect of propranolol was studied on mucoprotein and mucoproteoses in gastric juice in pylorus ligated albino rats. Mucoprotein and mucoproteoses were studied. The results indicate that the carbohydrate-protein ratio of both mucoprotein and mucoproteoses is significantly decreased by propranolol in 1 mg i.p. dose and significantly
increased with 50 mg i. p. dose of the drug. This increase and decrease of these two mucin factors go simultaneously with decrease and increase in ulcer index and acidity in pylorus ligated rats induced propranolol. The results suggest a vital role of both mucoprotein and mucoproteoses in gastric ulceration by propranolol.

80. Study of Paracetamol on Gastric Tissue of Guineapigs

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It has been reported that non-narcotic analgesics often produce gastric lesions in men and experimental animals. But paracetamol is often claimed to be free from such adverse effects though we reported that paracetamol induces dose dependent gastric lesions in guineapigs. The present study was undertaken to evaluate the effect of the drug on gastric tissue in guineapigs. It has been observed that paracetamol in 200 mg/kg dose produced well marked naked eye gastric lesion including ulceration. An attempt has been made to study the mechanism of the ulcerogenic property of the drug by estimating histamine and 5-HT content of gastric tissue and also acidity, pepsin and mucin content of gastric juice. It has been observed that while pepsin and mucin content of gastric juice showed an increase, both the free and total acidity decreased significantly. Histamine content of gastric tissue showed no alteration whereas the 5-HT content reduced significantly. Thus it may be assumed that 5-HT liberated from gastric tissue and the increased pepsin content may probably be the factors involved in the causation of gastric lesions. Literature survey reveals an increased pepsin content and mucin content of gastric juice after the administration of 5-HT. We have used methysurgide a 5-HT antagonist and found that it has failed to protect paracetamol induced gastric lesions.

81. Pharmacological Analysis of Stress-Induced Gastric Ulceration in Rats

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Forced immobilization produced acute gastric ulceration. A combination of immobilization and exposure to cold stress (4°C) produce the gastric ulceration more quickly. Interacerebroventricular (i.c.v.) administration of 6-hydroxydopamine
and atropine significantly blocked the restraint ulceration. MAO-inhibitor J. B.-516 (i.c.v.) enhanced the incidence of restraint ulceration. Vagotomy and spinal transection significantly reduced the incidence of restraint ulceration, whereas bilateral adrenalectomy failed to block it. Intraperitoneal pretreatment with dibenamine, atropine or metiamide significantly reduced the stress-induced gastric ulceration while mepyramine and cyproheptadine failed to do so. The mechanism of stress-induced gastric ulceration will be discussed.

82. A Method of Production of Gastric Ulcer in Animals by Cerebellar Lesion

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The effect of discrete vermel lesion of the cerebellum on the basal gastric secretory response was examined in unanesthetized unrestrained, conscious cats (15) and 42 rats of both sexes equipped with a permanent indwelling gastric cannula. A second group of animals (18 rats and 6 cats) similarly prepared with indwelling gastric cannula without any cerebellar lesion were subjected to cold stress. Routine analysis of gastric juice for total volume, acid output and pepsin concentration were undertaken for three weeks after complete recovery from surgery. The total volume and acid output were consistently more increased in cerebellar lesioned animals while they were markedly decreased in cold stress induced animals. Both the mean value of pepsin output and concentration were significantly decreased in both groups. Histopathological studies of autopsied stomach showed large ulcers with petechial haemorrhages confined in glandular and ruminal part in cerebellar lesioned animals while small ulcers scattered along peripheral part of stress induced stomach.

83. Effect of Female Sex Hormones on Experimentally Induced Acute Gastric Ulceration

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Effect of estrogen and progesterone was studied on experimental gastric ulceration induced by (a) stress, (b) Pyloric ligation, and (c) histamine and also on basal gastric acidity and peptic activity. They were found to protect animals against experimental gastric ulceration induced by histamine and pyloric ligation but not against stress induced ulceration. Their antiulcer action could not be correlated with their effect on gastric acidity or peptic activity.
84. Stimulation of Gastric Secretion by Prostaglandin $F_2\alpha$

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The effect of prostaglandin (PGF$_2\alpha$) on basal gastric secretion was investigated using gastric cannulated conscious alert rats. The gastric secretory volume, total acidity and pepsin output were routinely analysed at regular intervals before and after s.c. administration of PGF$_2\alpha$ at varying doses. PGF$_2\alpha$ produced an increase in gastric secretory volume, total acidity and pepsin content within one hour, while the PGF$_2$ showed a concurrent decrease in secretory volume and total acid output. The stimulant effect of PGF$_2$ was reversed by pretreating the animals with PGF$_2$. The maximum stimulant action of PGF$_2\alpha$ was seen at 200 $\mu$g and minimum was at 50 $\mu$g/kg doses, while doses above 400 $\mu$g/kg showed a decline in both acid output and total secretory volume. Analysis of the data demonstrated a clear dose-response relationship in the stimulant action of PGF$_2\alpha$. It is concluded that the two different components of prostaglandin (E$_2$ and $F_2\alpha$) act differently, while the known inhibitory effect of PGE$_2$ is confirmed, PGF$_2\alpha$ has got an excitatory effect on gastric secretion.

85. Further Studies on the Possible Role of Prostaglandin and 5-Hydroxy-Tryptamine in Gastric Ulceration

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In an earlier communication a possible role of prostaglandin and 5-hydroxytryptamin in the regulation of gastric secretion was reported. Prostaglandin E$_1$ was shown to increase the 5-hydroxytryptamine turnover of the pyloric antrum of stomach without affecting that of intestine. In the present study the effect of few prostaglandin synthesis inhibitors has been studied on the 5-hydroxytryptamine concentration in the rumen and glandular areas of the stomach of albino rats. 5-Hydroxy-indole-acetic-acid has also been estimated in the 24 hr urine. 5-Hydroxytryptamine has been estimated photofluorometrically. The concentration of 5-hydroxy-indole-acetic-acid was also determined. To find out a possible relationship with the stomach tissue concentration of 5-hydroxytryptamine and gastric ulceration, pylorus was ligated for 4 hr and ulcers were produced. The results show that all the prostaglandin synthesis inhibitors studied viz. aspirin, salicylic acid, indomethacin and diclofenac sodium caused an increase in the ulcer index along with a significant decrease of tissue
5-hydroxytryptamine in the glandular area, there being no significant change in the tissue 5-hydroxytryptamine in the rumen. 5-Hydroxy-indole-acetic acid excretion was found to be significantly decreased with all the drugs used. The present findings appear to be in conformity with the earlier suggestion that the inhibitory effect of prostaglandins on gastric secretion and ulceration might be mediated by 5-hydroxytryptamine.

86. Role of Gastric Juice Mucin in Peptic Ulceration-A Clinical and Experimental Study

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Role of mucin in peptic disease was first suggested by Claud Bernard and since then many workers have studied it either biochemically or histologically. These studies have been conducted mostly on experimental animals. Menguy and his co-workers have studied the problem in great detail by estimating the carbohydrate and protein in the nondialysable lyophilised fraction of the gastric juice and mucosa. In the present study the total carbohydrate content and the proteins have been studied in the alcohol precipitated fraction of the gastric juice both in experimental animals and in man. The results have been compared with those of nondialysable and lyophilised fraction of the gastric juice. The results of the present study indicate that there is no qualitative difference in the information obtained by these two methods both in experimental animals and in man. Further study shows that the carbohydrate protein ratio is significantly decreased in duodenal ulcer patients and in experimental ulcerations induced by aspirin, indomethacin and diclofenec sodium in albino rats. The acid-pepsin did not show any significant change by these drugs in the rats. Vegetable banana supplemented diet to these drug treated animals for two and seven days not only decreased the ulcer index by these drugs but also increased the carbohydrate-protein ratio indicating an increase in the total dissolved mucin. Aluminium hydroxide was used in these studies as the standard reference drug.
INDIGENOUS DRUGS

87. Cardiac Stimulant Effect of *Randia Dumerorum*

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A saponin was extracted from *Randia-dumerorum* fruits and subsequently purified into a stimulant and a depressant fraction. The stimulant fraction is further found to contain at least two active fractions. Both these fractions caused increase in amplitude of contraction of isolated frog and rabbit heart in doses ranging 1 to 2 microgram. The effects were comparable to those observed with adrenaline in 1/10 of the doses. The effect was blocked by propranolol. These fractions also cause marked potentiation of the broncho-dilator response of adrenaline in doses of 0.001 microgram. The saponin fraction also caused a constrictor response of the rat seminal vesicle. The other depressant fraction from the same plant caused inhibition of heart in $0.8 \times 10^{-8} \text{g}$. The saponin isolated from this plant seems to be of high biological activity and needs further detailed investigations.

88. Phytochemical and Pharmacological Study of *Caesalpenia bonduc*

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*Caesalpenia bonduc* (Latakaranj) leaf extract is used by ayurvedic physicians in patients suffering from bronchial asthma. As no detailed study of phytochemistry and general pharmacology has been reported, the present study was undertaken. Phytochemical analysis of *Caesalpenia bonduc* revealed the presence of alkaloid, glycoside, sterols, resins, gums, saponin and volatile oils. The alkaloid possessed relaxant action on bronchial muscles and smooth muscles of intestine and uterus. It was found to have hypotensive action which appears to be due to the direct vasodilator action. Further experiments showed depressant action on C. N. S. Thus alkaloid had significant action on cardiovascular and central nervous system. The results shall be discussed and presented.
89. Preliminary Pharmacological Studies on Delphinium denudatum

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The Pharmacological action of aqueous extract of Delphinium denudatum root was studied on the arterial blood pressure and respiration of dog, rectus abdominis and isolated heart of frog and smooth muscle of guineapig ileum. The drug did not show any significant effect on respiration, it shows a hypertensive action similar to that of adrenaline in dogs. This hypertensive action was blocked by tolazoline hydrochloride 10 mg per kg body weight. The drug gives prominent fall in blood pressure like adrenaline after alpha receptors were blocked. This fall was blocked by propranolol 2 mg per kg body weight. The extract increases both rate and force of contraction of the isolated frog heart in the doses of 10 mg per ml. The drug produces contraction on rectus abdominis of frog in the doses of 20 mg to 100 mg. This effect of drug was completely abolished by tubocurare. It also shows the contraction on smooth muscle of guineapig ileum which is not blocked by atropine or antihistamine.

90. General Pharmacological Study of Crataegus Oxycantha

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Tincture Crataegus oxycantha is used by homeopaths in patients suffering from congestive cardiac failure. It is also mentioned as cardiotonic drug in ‘Clinical Pharmacology’ by Dilling. The present study was undertaken as no detailed experimental work has been reported. Tincture Crataegus was found to reverse the cardiac depressant action of potassium on isolated frog heart experiments when perfused with frog ringer solution and oxygen lack in isolated guineaepig auricle. The results shall be discussed and presented.

91. Cardiovascular Effects of Aqueous Extract of Adonis vernalis

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Tincture Adonis vernalis is used by homeopathic physicians in patients suffering from congestive cardiac failure. In homeopathic repertoire its action has been
described very much similar to digitalis on heart. The detailed report on *Adonis vernalis* is not available; hence the present study was undertaken with both aqueous extract and tincture of *Adonis vernalis*. Aqueous extract of *Adonis vernalis* was found to have cardiac stimulant action on isolated heart preparations. It showed protection against heart failure produced by excessive load and high potassium concentration. Tincture *Adonis vernalis* was found to cause cardiac depression which was not blocked by the atropine. In isolated guinea pig auricle and rabbit auricles the drug increased the threshold of electrical stimulation. On dog blood pressure responses varied with dose, showed rise in blood pressure where as larger doses showed fall in blood pressure. The drug was also seen for effect on other systems in laboratory animals. The results shall be presented and discussed.

92. Diuretic Action of *Tinospora cordifolia*

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*Tinospora cordifolia*, an indigenous drug locally known as gul-wel has been found to have several useful pharmacological actions. The hypoglycaemic actions of this drug was reported earlier. There is also an isolated reference that a high concentration of this drug produced marked diuresis. This present study has therefore been undertaken to evaluate the diuretic property of *Tinospora cordifolia* in rats & dogs, and also its effects on the electrolyte composition of urine. It has been found that the drug produces a marked diuretic effect in both the species. The mean control urine volume before and after treatment in the dogs 58.5 ml and 175 ml, and in the rats was 5.4 ml and 17 ml. There was also a marked alteration in the Na, K and Cl levels in urine as compared to the normal samples. The comparative studies with known diuretic drugs are in progress.

93. Pharmacological Studies on Aporphine Alkaloids from *Croton sparsiflorus*

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Bhakuni and co-workers in 1970 isolated an already known aporphine alkaloid, sparsiflorine (I) from *Croton sparsiflorus* and prepared its two semisynthetic derivatives-N-methylapocrotosparine (II) and N-methylapocrotosparine methiodide
Hypotensive effect of a proaporphine alkaloids isolated from *C. sparsiflorus* was reported earlier. Proaporphines are biogenetic intermediates of aporphine alkaloids and these aporphine alkaloids had similar hypotensive effects. At 5-10 mg/kg doses they produced 40-60 mm Hg fall in blood pressure of anaesthetized cats. The duration of hypotension was 15-60 minutes with I and 60-90 minutes with II and III. Adrenaline induced pressor response was either reversed or inhibited. The α-adrenergic blockade seems to be mainly responsible for the hypotensive response in all the cases. N-methylapocrotsparine methiodide, also showed marked (66-100%) neuromuscular blockade at 5 and 10 mg/kg dose on gastrocnemius muscle-sciatic nerve preparation of cat. The neuromuscular block was completely reversed by neostigmine.

**94. C. N. S. Activities of *Semecarpus anacardium* Linn**

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The oil fraction of *Semecarpus anacardium* Linn was undertaken for pharmacological screening. Initial general behavioral study showed some C. N. S. activities, which were further confirmed by simple tests. The results of observations will be presented and discussed.

**95. Preliminary Report on Pharmacological Studies of *Mollugo carviana***

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The herb *Mollugo cerviana* of the Molluginaceae (Sanskrit-Kannana. Tamil-Parpataka, Hindi-Pitpapda) is considered as stomchic, antiseptic, laxative, febrifuge and diaphoretic. An infusion of the plant is given to promote lochial discharge. Oil in which roots are boiled is used as an application for gout and rheumatism. An alcoholic extract of the plant shows antibacterial activity against escherichia coli and is used as a cure for gonorrhoea. It appears no attempt has been made to screen this plant to test the validity of claims made. Hence extract of whole plant has been studied for its activity on C. V. S. and various smooth muscles. Preliminary results of this study will be reported.
96. Hypotensive Action of Flowers of Anchusa strigosa (Gaozeban)

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The hypotensive effect of the aqueous extract of Anchusa strigosa flowers was reported by us earlier. This report being of preliminary nature, the present investigation was undertaken to study its effect in detail. The aqueous extract of the drug (100 to 200 mg/kg, i.v.) in anaesthetised dogs produced hypotensive effect for more than half an hour after an initial transient rise. The lethal dose in dog was found to be 4g/kg, i.p. The ALD, in mice was 2g/kg, i.v. This indicates a good safety margin. The hypotensive effect was not blocked by atropine or mepyramine maleate. The extract failed to modify the effect of acetylcholine, histamine or epinephrine. Its effect was not altered in spinal dogs. The extract has no significant effect on isolated frog heart. However, the extract was found to have slight inhibitory effect on the auricular contraction in bilaterally vagotomised dog but there was no effect on ventricular contraction in this animal. The above results indicate that the site of action is probably blood vessel which is being studied. The extract was devoid of anticonvulsant and analgesic properties.

97. Some Pharmacological Actions of the Extract of Hygrophila spinosa

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The root, leaves and seeds of the plant Hygrophila spinosa have been reported to be useful in dropsy, stone in the kidney and in rheumatism in the ayurvedic literatures. A pharmacological study of the alcoholic extract of the leaves of the plant was made. The extract produced sedation, and prolongation of hexobarbital-sleep time but was devoid of any significant analgesic and anticonvulsant activity. It produced depressant effect on isolated perfused frog and mammalian heart preparations, lowered blood pressure of anaesthetised dogs and enhanced perfusion rate in frog vascular system. ICV administration of the extract in anaesthetised dogs reduced blood pressure and reflex pressor responses. The extract also relaxed smooth muscle preparations and antagonised the contractile effects of histamine, acetylcholine and barium chloride on these preparations. A moderate diuretic effect of the extract was observed in rats and anaesthetised dogs. The significance of these observations will be discussed,
98. **Relaxant Effects of Cold Aqueous Extracts of *C. Copticum* seeds**

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Infusions of *C. Copticum* (Omum) fried seeds are used in the control of diarrhoea in the indigenous medicine. We have shown that hot extracts from omum seeds or extracts from fried omum seeds contain large amounts of acetylcholine and choline. These extracts were found to mimic all effects of acetylcholine both nicotinic and muscarinic. Cold extracts from the *C. copticum* seeds were found to have a relaxant action on gastro-intestinal tract. Omum water is used as an anti-spasmodic in gripe in children. In the present study the relaxant actions of cold omum aqueous extracts are investigated. On the rat alimentary tract the omum extract \((OE,)_c\) produces only relaxation whereas choline and thymol which are its other constituents produce stimulation. The acetylcholine, histamine and barium chloride induced contractions are depressed to the same extent and is limited only to the contraction immediately following application of the omum extract. So it is not like antiacetylcholine, or antihistamine or papaverine. Its relaxant action cannot be sympathomimetic because it produces fall of blood pressure in cat, dog and rat. On the isolated frog’s heart the extract produced an initial depression and subsequent stimulation. The stimulation was not antagonised by propranolol and the depression by atropine. The results will be discussed.

99. **A Pharmacological Evaluation of Anti-Pyretic, Analgesic and Anti-Inflammatory Activities of Some Indigenous Drugs**

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In the present study 70% alcoholic extracts from Hibiscus *rosa-sinensis* (leaves), *Withania somnifera* (dafatted seeds), *Tephrosia purpurea* (whole plant), *Nigella sativa* (seeds) and the pure glycoside obtained from the roots of *Nerium indicum* (Plumieride) were studied for their antipyretic, analgesic and anti-inflammatory activities. Among these drugs, the extract from *Hibiscus rosa-sinensis*, Pure glycoside from *Nerium indicum* and *Withania somnifera* showed the presence of potent antipyretic, analgesic and anti-inflammatory activities \((P<.001)\) in albino rats and mice. Since, the extracts have low toxicity and high safety margin, they may be assessed for their usefulness in ayurvedic system of medicine in cases of fever, pain and rheumatism.
100. Preliminary Pharmacological Studies of Three Flavonoid Glycosides of Plant Origin

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These flavonoid glycosides, swertisioside (Eh), hoppioside (Hd) and swerticytisoside (Sb), obtained from Enicostemma hyssopifolium (Willd.), Hoppea dichotoma (Willd.) and Swertia bimaculata (Hf. & T) respectively, were studied on isolated frog heart, smooth muscles of rabbit, rat and guinea-pig and anesthetized dog blood pressure, respiration and E.C.G. pattern. Hd, Eh and Sb (lo-200 Pg) precipitated cardiac arrhythmias in perfused frog heart and produced positive ionotropic response on perfused hypodynamic frog heart. On Straub’s ventricle preparation, Eh was the most potent and Sb the least potent. The three glycosides (20-50 mg/kg) produced hypotensive action in dog, the effects being prolonged with Eh and Sb. Respiration rate decreased with Eh and Sb and increased with Hd. In high doses, the three glycosides produced depression of R wave and a slight inversion of T wave. Hd caused contraction of guinea-pig ileum which was blocked by pentolinium and atropine whereas Sb antagonised the actions of histamine and acetylcholine. On rabbits intestine, Hd inhibited the pendular movements which was unaffected by beta adrenoceptor blocker, Sb caused contractions which was blocked by atropine. All the three glycosides antagonised the action of carbachol on rat uterus. On guinea-pig vas-deferens Sb and Eh potentiated the responses of adrenaline, while Hd produced adrenalineline-like response blocked by phentolamine.

101. Phytochemical and Pharmacological Study of the Plant Jatropha curcas (Linn)

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Phytochemical and pharmacological studies with the fruits of Jatropha curcas Linn, were undertaken. The epicarp was subjected to different extractions and determination of ash and mineral contents, sugar, steroids, resin, saponin, tannin, glycosides, alkaloids and the seeds for fixed oil. The alcoholic extracts-Fraction I and II, aqueous, chloroform, petroleum ether and benzene extracts of the epicarp were studied for their actions on cardiovascular system, plain and skeletal muscles, blood and inflammatory reactions and the seed oil for its purgative and other effects on the gastro-intestinal tracts. The alcoholic extract
ABSTRACTS

contained active principles producing hypotension, cardiac depression, spasmodic effect on smooth and skeletal muscles. It induced inflammation in rabbit conjunctiva and rat hindpaw. The faction II increased prothrombin time in rabbits. The chloroform extracts produced mild stimulation of the isolated frog heart while the petroleum ether and alcoholic extracts were found to produce a marked hemolysis of human erythrocytes.

102. **Pharmacology of *Moringa olifera***

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*Moringa olifera*, an indigenous plant, has been used in ancient medicine for various ailments. The roots and bark contain three alkaloids moringen, moringenine and spirochene and has been shown to have vasopressor effect on B. P., cardio-accelerator effect and depressor effect on smooth muscle of intestine and bronchus in various animals. Lay-press reports in Burma have described the use of leaves of this plant in hypertension. These tempting reports have prompted us to undertake a detailed study of the leaves of this plant. Serial extracts of *Moringa olifera* were prepared in petroleum ether, benzene, ether, chlorform, alcohol and water and were tested on various tissues *in vitro* and some preparations *in vivo*. The extract of the leaves of this plant has a depressant action on the heart and produces a fall of B. P. in dogs. The details of the pharmacology of this drug will be reported.

103. **Antifertility Activity of *Embelia ribes* (*Burm)* Seeds in Female Rats**

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*Embelia ribes* (Sans, Vidanga; Family Myrsinaceae) has been attributed to possess antifertility activity in ancient ayurvedic literature. Although its potent contraceptive action has been claimed by ayurvedic physicians, studies in experimental animals have given inconclusive results. In the present communication, the antifertility activity of the crude material as well as the aqueous and alcoholic extracts, has been reported in female rats. Incorporated into the diet at various dose levels and administered to female rats, the crude material showed 60% antifertility activity. The alcohol and aqueous extracts however failed to show any significant effect on the estrus cycle, mating behaviour and fertility of the rats.
104. Studies on the Pharmacological Effects of “Placentrex”
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Placentrex, a fresh sterile aqueous extract of human placenta manufactured by M/s Albert David Limited has been claimed to be effective in the treatment of several diseases, such as ulcers, cirrhosis of liver, atrophic rhinitis, and inflammatory diseases. Hence systematic pharmacological study was undertaken to elucidate the probable beneficial effects on experimental animals. In rats placentrex increased the tensile strength of the healing wound. It exerted anti-inflammatory effects as tested by cotton pellet implantation technique and mild analgesic effect as tested by hot plate method in rats. In partial hepatectomised rats administration of placentrex increased the rate of liver regeneration as evidenced by the increase in mitotic index in the 5th and 7th post operative days. Parenteral administration of placentrex did not produce any significant changes in the CNS and CVS of various laboratory animals. In very high doses it produced non-specific antagonism of smooth muscle stimulants.

105. Studies with Embelia Ribes in Male Bounet Macaques
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The antifertility of an indigenous preparation ROC 101, in male mice has been previously reported (Munshi and Rao, 1972). It is an ayurvedic preparation composed of Embelia ribes (Vidanga), Piper longum (Pippali) and Borax (Tankana). Our recent studies have revealed that Embelia ribes is the most potent component of this preparation in rodents when given separately. Studies were therefore undertaken to evaluate its activity in male monkeys. Embelia ribes berries were powdered and administered in the diet for 90 days. Semen and blood samples were collected at weakly intervals during the entire study. The results revealed considerable decrease in volume of the semen, sperm motility and testosterone levels. Spermatogenesis was normal as revealed by testicular biopsy at the end of the treatment period. The results suggest an action of the plant on the accessory sex organs.
106. Membrane Stabilizing Effect of Indoline-2,3-dione

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Indolines-2, 3-dione has been reported to protect rats against maximal electro-shock seizures. The present study was taken up with a view to ascertain whether indoline-2, 3-dione had a membrane stabilizing effect. The membrane of the isolated frog sartorius muscle was rendered hyper-excitable by any one of the following three procedures: bathing the isolated muscle in Ca++ free bicarbonate buffer solution or adding veratridine (3x10^{-7} w/v) or aconitine (10^{-5} w/v) to the buffer. Indoline-2, 3-dione (10^{-4} w/v) completely antagonised the augmented muscle response to a single supramaximal stimulus during the above procedures. These findings are suggestive of a membrane stabilizing effect of indoline-2, 3-dione.

107. Effect of Cyclophosphamide on Mast Cell Regeneration and Distribution

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The effect of a cytotoxic drug cyclophosphamide on mast cells was studied. Both acute and chronic treatment and its effects were studied. Albino rats injected with normal saline were used as control animals. The drug was injected in thymectomised and sham-thymectomised animals. In acute treatment the animals were sacrificed 24 hours after a single injection of the drug and the mast cells counted in all the groups. In chronic treatment the animals were injected for 5 consecutive days with the drug and sacrificed after 48 hours, 72 hours, 5 days and 7 days. Mast cells in various tissues were counted. The results will be discussed.
Further Studies on the Mechanism of the Hypoglycemic Effect of B. Pertussis Vaccine

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Preliminary studies on the mechanism of hypoglycemic action of B. Pertussis vaccine have been reported by us earlier. The presence of an intact pancreas is essential for its maximum hypoglycemic action and like insulin the vaccine also increases the glycogen levels in various tissues. In the present work the effects of the vaccine on alloxan induced diabetes in rats, arteriovenous glucose difference in rabbits, free fatty acids in rats & glucose tolerance curve in rats were studied. It is observed that the vaccine potentiates the hypoglycemic effect of insulin on alloxan induced hyperglycemia produces a greater fall in the blood sugar in the vein as compared to the artery, lowers the free fatty acids and the effect on the glucose tolerance curve resembles that of insulin. This shows that the vaccine has an insulin like action. However a beta blocking action may also contribute to hypoglycemia. Further work is in progress.

Biochemical Changes During Endotoxin Shock in Rats

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It is known that acute endotoxin shock is characterized by a number of haemodynamic and biochemical changes. From our own laboratory we have reported some of these haemodynamic alterations during endotoxin shock in dogs. The present study was initiated to understand various biochemical changes like blood sugar, liver glycogen, serum free fatty acids, serum glutamic oxaloacetic and pyruvic transaminase, adrenal ascorbic acid, and levels of catecholamines in adrenal glands and heart during endotoxin shock in rats. It was observed that lyophilized extract of E. Coli endotoxin (10 mg/kg I. P.) produced mortality in 8 hours in 60% of animals. Hence, it was decided to investigate biochemical changes (as mentioned above) occurring in rats 6 hours after the administration of endotoxin. The results indicate insignificant decrease in blood sugar accompanied by significant decrease in liver glycogen. Serum transaminase activity were significantly increased, indicating pathological changes in cardiac tissue as well as in liver presumably due to haemodynamic changes in circulation. Adrenal ascorbic acid was markedly lowered probably indicating stressful condition of the animal and an enhanced synthesis of gluco-corticoids. Serum acid phosphatase was moderately increased probably due to an earlier haemodynamic changes or
secondary to increased kinin or kallikrein activity. There were no significant changes in adrenal catecholamine levels, possibly due to an increased turnover rate of catecholamines. We believe, that endotoxin induces stressful condition which will lead to biochemical sequelae detrimental to their survival.

110. Effect of Intrathymic and Subcutaneous Injection of TAB Vaccine on Tissue Mast Cell Count in Albino Rats

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In our study an interrelationship between thymus and mast cells, we have already reported an increase in mast cell count in thymus and other tissues at distant sites following intrathymic injection of a chemical carcinogen in albino rats. To study further this interrelationship, the present work was undertaken. Mast cell count in thymus and other tissues was made following intrathymic as well as subcutaneous injection of another antigenic substance-TAB vaccine. In addition histological study on thymus and lymph node was also made. The observations made were compared and their significance will be discussed.

111. Phenyl Phenacyl Bromide of Heliotridane: A New Potent Non-Specific Antispasmodic

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A number of semisynthetic quaternary pyrrolizidines based on pyrrolizidine alkaloids condensed with alkyl halides were developed and investigated pharmacologically. These showed varying degrees of non-specific type antispasmodic activity. 4-phenyl phenacyl bromide of heliotridane was most potent of the series. The base heliotridane was obtained by hydrogenation of 1-methylene pyrrolizidine obtained from Crotalaria anagyroides. The antispasmodic activity of this compound have been investigated on rat colon and guinea-pig ileum against different spasmogens and rabbit duodenum in vitro and by charcoal meal test in mice and jackson’s enterograph on dog intestine against the spasms induced by carbachol and morphine. The antispasmodic activity of 4-phenyl phenacyl bromide of heliotridane was of non-specific nature like that of papaverine and was more potent than the latter.
112. Studies on Pigment Formation During Tryptamine Oxidation by Guinea-pig Liver Mitochondria

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The production of pigments from amines in animal tissues appears significant since it has been suggested that some of these pigments may be associated with certain type of mental diseases. Our knowledge on the biochemical reactions leading to the formation of pigments from indole-alkylamines is very meagre. A method for quantitative estimation of pigment formation during tryptamine oxidation by guinea-pig liver mitochondria is described. The enzymatic reaction was found to be linear up to 120 min of incubation time end 50 mg of tissue (wet wt.). The pH-optimum was found to be 7.5. Liver and kidney tissues exhibited increased rate of pigment formation in comparison to brain and intestine. The pigment forming reaction was found to be oxidative one but does not require high partial pressure of O₂. Among the various tryptamine derivatives studied, 5-methoxy-tryptamine was found to be the best substrate. Various potent monoamine oxidase inhibitors like pargyline, clorgyline, tranylcypromine, catron etc. inhibit pigment formation strongly. p-CMB, N-ethylmaleimide and heavy metal ions like Hg²⁺, Ag⁺, Cu²⁺ inhibit pigment formation, indicating the possible involvement of -SH group in the active site of the enzyme responsible for pigment formation. Thin layer chromatography of the ether extracted pigment shows complete absence of indole-acetic-acid in the reaction product.

113. Monoamine Oxidase inhibition Patterns in Sub-fractions of Rat Brain Mitochondria by Clorgyline 8 Chlorophenoxy-Cyclopropylamine

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Recent studies indicate functional heterogeneity of brain mitochondria. Rat brain mitochondrial fraction as is routinely prepared by the method of differential centrifugation is grossly contaminated with myelin fragments, ruptured membranes, cholinergic & adrenergic nerve-ending particles etc. In vitro studies with crude mitochondrial fraction therefore yield summated activity of all the above-named subcellular particles along with the free mitochondria. By the use of sucrose density gradient centrifugation technique the crude mitochondrial fraction can be sub-fractionated into five parts-three of which contain appreciable monoamine oxidase (MAO) activity. They are the free mitochondria of the
perikaryon, cholinergic synaptosomes and adrenergic synaptosomes. The present work indicated that type A and type B MAO are distributed in different ratios among these three sub-fractions. Clorgyline & chlorophenoxy-cyclopropylamine, two of the so-called selective MAO inhibitors which discriminate between type A & B MAO were used to characterise the MAO activities of these three subfractions of brain mitochondria. *In vivo* and *in vitro* inhibition patterns of MAO with tyramine and serotonin as substrates were studied with the above two drugs.

114. Studies on Some Aspects of Contact Lens Solutions

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Contact Lens solutions containing suitable viscosity building agents, surfactants and preservatives were formulated. Changes in physicochemical properties of the solutions after aging, autoclaving and refrigeration were studied. The effects of tonicity, pH and Tween-80 were also studied. The various findings will be discussed.

115. Survey in Prescribing Trends in Nursing Homes of Delhi

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A sample survey of trends in prescribing in North, Central and West zones in city of Delhi was made. A total of 764 prescriptions obtained from records of indoor patients of 17 nursing homes were found to contain 3225 drugs. Almost all the prescriptions had more than 1 drug with a range of 2-17 and the average being of 4 drugs per prescription. Information about age, sex, provisional diagnosis, strength of dosage form, instruction to patients and duration of therapy was conspicuously absent in the recorded prescription. Drugs were categorised into 15 groups and most frequently prescribed groups of drugs were anti-infective 25%. multivitamins and haematinics 16.4%. analgesics 15.9%. tranquillisers 10.15%. 25 prescriptions were found to contain same generic drugs prescribed under garb two different trade names. Some groups of drugs were
prescribed under a variety of fanciful trade names (multivitamins, haematinics and cough remedies and bronchodilators, digestants, antacids, tranquilizers, anti-tubercular agents, steroids) and collectively grouped as miscellaneous in which included 40-67% brand drugs. Thus preference to a particular brand name was not adhered to. Brand drugs manufactured by multinational pharmaceutical houses were generally preferred. Popularity of drug was determined by counting the number of times it appeared in the prescriptions analysed. Most popular drugs amongst anti-infective group was resteclin & septran; in multivitamin group-surbox-T; in analgesics-pethidine & novalgin; in tranquillizers-siquil and calm-pose; in bronchodilators-deriphylline, in antihypertensives and diuretics-lasix & in steroids-decadron. The survey has highlighted some of the prescribing trends in general practice, particularly in Delhi nursing homes, which may have medical, financial and social implications.

116. Variation of Prothrombopenic Effects of Warfarin in Rats due to Environmental Factors

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The prothrombopenic activity of warfarin show pronounced variations in their elimination kinetics in man and in animals. These variations are usually explained in terms of interindividual differences in the activity of drug metabolising enzymes due to genetic or environmental factors. The concentration of free warfarin in plasma is well correlated with the anticoagulant effects and its rate of clearance. The characteristic of plasma protein binding of warfarin in rats are better matched to pharmacokinetic models than those of the clinical patients on warfarin. Rats captured from the natural habitat were used in the present investigation to compare the environmental factors determining the anticoagulant effect of warfarin. CF rats bred in the controlled environment of animal house were used parallelly. Warfarin was administered through either food or drinking water to minimise handling of animals. CF rats showed prothrombopenic effects of warfarin at very low dosage (0.45 ppm in water) whereas rats from natural habitat were nonresponsive. Warfarin was lethal (10 ppm in water) in rats in captivity. The wide variation in metabolic status indicated by blood glucose, liver glycogen, serum protein and drug metabolising enzyme activity along with variation in adrenal function indicated the importance of the environmental factors which continued to influence the efficacy of warfarin. A distinct difference in response to warfarin between male and female rats was also observed.
117. **Some Studies on Glycoproteins and Glucose in Amniotic Fluid**

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The reported studies on glucose level in the human amniotic fluid show contradictory results; while no significant difference between preterm and fullterm has been reported, others showed a decrease of the glucose level in fullterms. As far as could be ascertained from the available literature no studies appear to have been made on the glycoproteins of the amniotic fluid in different period of gestation. In the present study, the glycoproteins were estimated in terms of its total carbohydrate content in the alcohol precipitated material of the amniotic fluid by the usual methods. Glucose was estimated by Folin Wu’s method. The results of the present study indicated that the glucose level in the amniotic fluid obtained from the fullterms (over 37 weeks) is significantly low compared to those obtained from preterms and there is a significant negative correlation with gestation. The total carbohydrate (after estimating the individual carbohydrate components viz. total hexoses, hexosamine, fucose and sialic acid) level in the glycoproteins of the amniotic fluid, on the other hand, shows a steady increase with the gestation and a significant positive correlation has been found. The estimated total proteins of the amniotic fluid also show a negative correlation. The results are difficult to interpret with the available data as no correlation could be found with protein and carbohydrate keeping gestation period as constant.

118. **Neuromuscular Blocking Activity of a New Series of Semisynthetic Quaternary Pyrrolizidine and their Structure-activity Relationship**

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A new series of semi-synthetic quaternary compounds (mono and bis quaternary) bases on the pyrrolizidine alkaloids, L-methylene pyrrolizidine, monocrotaline, retronecine and heliotridane showed varying degree of neuro muscular blocking activity resembling d-tubocurarine. The activity was investigated by a number of techniques in vitro and in vivo in frog, rat, chick, mouse, rabbit and dog, and was compared with that of d-tubocurarine. The ED₅₀ values and comparative potency of these compounds were determined. Their structure activity relationship study has shown that: (1) increase in the length of alkyl chain enhances the activity. (2) bromo derivatives were more potent that the chloro derivatives
(3) the exomethylene group at C, imparts more activity to the molecule than the methyl group at this position (4) bis-quaternization reduces the activity and (5) the derivatives of monocrotaline which have unsaturated necine base and are hepatotoxic are far less potent than those of l-methylene pyrrolitidine and heliotridane which have saturated necine base and non-hepato toxic.

119. A Behavioral Investigation on Sub-Sedation Dosage of Pentobarbitone

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The aim is primarily exploratory to see whether the administration of sub-sedation threshold value of pentobarbitone can give rise to behavioral index beneficial in human affairs. Six laboratory-bred littermate albino rats were intraperitoneally administered 10 mg/kg of pentobarbitone and distilled water of similar volume on alternate days for 20 days consecutively. Immediately after the treatment the animals were placed in a standard straight alley maze to run from the start box to the goal box for a block of 3 trials, which were over in an average of two minutes. The animals were given a rest period of ten minutes after the first block of trials, and thereafter, they were put to four blocks of trials similarly. The t-tests, within the last three blocks of trials, between the running time indices of the animals under drug and placebo treated conditions yielded significant differences beyond .05 level of confidence. Similar comparison of the over-all running time indicated significant difference between .06 and .05 level of confidence. All these computations indicated superiority of the drug treated over the placebo condition. The results will be discussed in the light of pharmacological aspect of psychiatry.

120. Effect of DDT Pretreatment on Malathion Toxicity in Chicks

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Pretreatment with DDT protected mice against the toxicity of organophosphate parathion but not against its active metabolite paraoxon. This is explained on the basis of an increased rate of conversion of parathion to the inactive product diethyl-phosphorothionic acid. An attempt has been made in this study to find out if similar treatment with DDT would protect chicks against malathion toxicity. The results showed that DDT pretreatment at the rate of 200 mg/kg had maximal
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protective effect on the 3rd day after treatment against malathion toxicity. The values for LD50 of malathion with and without DDT pretreatment in 21-day old chicks was 446.0 and 281.8 mg/kg respectively. Further studies are in progress to explain the mode of protection in chicks which is of practical significance in poultry industry.

121. Altered Drug Metabolic Pathways in Rats During Chronic Treatment with Oral Contraceptive

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Steroids are known to alter drug metabolism by inducing hepatic microsomal enzymes. As oral contraceptives are now widely used, we have studied the effect of chronic administration of the combination of oestrogen and progesterone (Lyndiol, Organon) on two different drug metabolic pathways, viz. acetylation and oxidation in female adult rats. Isolated liver perfusion technique has been used to study this effect so that only liver involved in drug metabolism. Chronic treatment with oral contraceptive markedly increased the acetylation process (acetylation of sulphadiazine) and oxidation process (oxidation of phenylbutazone). Increase in enzyme induction may be due to increase in turnover of microsomal proteins and this process may interfere with the therapeutic effects of certain drugs.

122. Some Preliminary Pharmacological Studies with Toxohormone Obtained from Horn Cancer of Bullocks

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One of our colleagues isolated and purified a chemical compound (toxohormone) from horn cancer of bullocks, commonly prevalent in this country. This compound is being investigated for its pathology, immunology and pharmacology. It was observed that animals dying of horn cancer showed severe constipation and impaction. In view of this observation some preliminary pharmacological studies with toxohormone were conducted. The compound produced mild sedation, decreased spontaneous motor activity and prolonged barbiturate sleeping time in mice. On isolated guineapig ileum toxohormone up to 0.5 \( \mu g/ml \) had no effect of its own, while Ach induced contractile response was inhibited in the presence of toxohormone. On isolated frog heart it caused both positive inotropic and chronotropic effects,
123. Exploration of Adenosine as Receptor site for Biomolecular Interaction of Amphetamine with RNA-XI

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As a result of nuclear magnetic resonance and infrared spectroscopic studies, it has been found that d-amphetamine interacts with RNA and ATP. Phenyl ring of d-amphetamine has been shown to interact with adenosine base due to stacking attraction and forms a reversible molecular complex with the electron acceptor sites of RNA. Methyl group of α carbon atom in d-amphetamine molecule appears more susceptible during RNA interaction than the methylene group of β carbon atom. A folded over side chain configuration of d-amphetamine molecule is proposed, while amino group is protonated. However, a steric change due to protonated or non-protonated amino group of the side chain has no influence on RNA or ATP interaction.

124. Innervated Straub's Heart Preparation

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Adrenergic neurone blocking activity is studied on various innervated Preparations. This simple modification of original straub’s heart preparation provides an economical and convenient method for studying these drugs in addition to the possibility of studying cholinergic neuro-effector transmission. The pithed frog is fixed dorsally on the frog board and its heart is exposed widely and cleared of its pericardium. The inferior and the two anterior venae cavae are ligated. A long-nozzled Straub’s cannula with its nozzle bent at right angle to its main body, is introduced into the ventricle through the cut in the left aorta and the right aorta is ligated. The ventricle is washed clear of its blood with Ringer solution. The apex of the heart is connected to a writing lever. The heart is kept moist and the oxygen is bubbled into the Ringer of the cannula. The vagus on the right side is briefly stimulated by a low volt-low frequency current which gives instant bradycardia or cardiac standstill. This can be easily blocked by atropine. An enhanced stimulation of the atropinised heart gives a stimulation of the heart which is adrenergic in nature as it can be selectively blocked by guanethidine and propranolol. The preparation is very simple, and can be used for screening or confirming guanethidine type activity. It is very economical in terms of the cost of animal and the drug needed, and the nerve does not come in contact with the drug.
125. Experimental Elicitation of Jaw-Closure Reflex and Lock-Jaw in Animals

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The linguomandibular reflex (LMR), as elicited by electrical stimulation of tongue, is widely employed to assess the central muscle relaxant activity of drugs. Even though LMR is considered to be a jaw-opening reflex, antagonism of strychnine of tetanus toxin induced facilitation of LMR has been employed to assess the antitetanus activity of drugs. It is conceivable that antagonism of jaw-closure rather than jaw-opening reflex should be employed to assess the antitetanus activity of drugs. In the present investigation an attempt has been made to develop an experimental technique for eliciting jaw-closure and jaw-opening reflexes separately. Electrical stimulation of the root of tongue elicits both jaw-opening (Lingua-digastric reflex, LDR) as well as jaw-closure (Linguo-temporomasseteric reflex, LTMR) reflexes. With this newly developed technique it is possible to record both these reflexes separately in a single animal preparation and study the effect (s) of drugs on these reflexes. It was interesting to observe that with the use of higher frequency of stimuli a state resembling “Lock-Jaw” as seen in case of tetanus can be produced in this experimental set-up.

126. A Simple Model to Study the Effects of Broncho Constrictors and Bronchodilators and to Estimate the Mediators of Allergy

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Several experiments have been carried out to study the pharmacological actions of bronchoconstrictors and dilators in perfused guineapigs. However, this species is costly end not easily available and takes at least 3 weeks for them to get sensitised. Rats were, therefore, selected for our experiments to study the allergic phenomenon as its lung tissue has a similar pattern to that of human beings. An added advantage is that the rat species are quickly sensitised, cheap and easily available. The method consisted in perfusing the fluid down the trachea through the bronchii and allowing to escape from alveoli through scratches on the surface of the lungs. The isolated rat lung tissue was perfused with Kreb’s solution and the perfusate collected in a levelling blub through a funnel and connected to the volume recorder via a T-tube: the excess fluid being allowed to drain after noting the maximum height (constant volume). 5-HT,
histamine, epinephrine and isoprenaline were added separately and changes in the rate of flow and quantity of substance in perfusate were recorded, using rat fundus and spectrophotofluorimeter. Results show that bronchoconstrictors like 5-HT and histamine decrease the rate of flow while bronchodilators like epinephrine increase the rate, and these are statistically significant. Increases in the dosage result in rise of its level in the perfusate.

127. Isolated Innervated Auricles of Frog for Neuroeffector Transmission Studies

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Innervated preparations, e.g. vas deferens, ilium, nictitating membrane, blood vessels etc. have been used for studying the physiology and pharmacology of adrenergic neuroeffector transmission. However, these experiments involve the use of costlier animals and more elaborated set-ups. The present communication describes a preparation which is dually innervated by cholinergic and adrennergic nerves, is economical and simple, doesn’t need elaborate set-ups and does not need to be dissected and mounted with great speed as in mammalian hearts. The pithed frog (150-250 g) is secured dorsally on the frog board. Its abdomen is opened, sternum excised away widely. the heart exposed well and pericardium removed. The Vagus nerve on one side (usually right) is cleaned, severed proximally and its end secured in a ligature. The nerve alongwith the heart and the intervening tissue is dissected out and transferred to a petridish containing frog Ringer solution. Ventricle is cut away and the nerve-auricles are mounted in the isolated organ bath with the nerve placed on a pair of electrodes. Stimulation of the nerve at low frequency and voltage produces immediate bradycardia or cardiac standstill which is cholinergic in nature. A relatively higher frequency and voltage stimulation of the atropinised preparation produces a marked cardiac stimulation which is adrenergic in nature as guanethidine and beta blockers can block it selectively. Thus unatropinised preparation can be used for cholinergic, and atropinised preparation can be used for adrenergic neuroeffector transmission studies, specially as an economical simple method of screening and confirming guanerhidine like activity.
A Simplified Organ Culture Technique for Production of Enzymes by Human Placenta: Effect of Oxytocin

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Normal human placentae (10 to 20 weeks gestation) were collected at the time of hysterotomy and prepared under aseptic conditions for organ culture. For this purpose, 25 to 30 fragments (1 mm³ size) of normal villi were placed on a filter paper supported on glass beads in a petridish containing 5.0 ml of culture media, and kept in a humidity chamber (an air-tight glass jar) which was aerated with 95% O₂ and 5% CO₂ at 8-hr intervals. About 10 to 12 such jars were put for incubation at 35° to 36°C for each experiment. Random samples of tissue fragments were taken periodically for histological examinations as well as for quantitative estimations of enzymes-oxytocinsse, heat stable alkaline phosphatase (HSAP); acid phosphatase and protein in both incubation medium and tissue fragments. Oxytocin (Syntocinon) at a concentration of 200 mIU/ml was added into the culture medium 24 hours after initial culture and its effect on production of these parameters observed on day 1, day 2 and day 3 of oxytocin treatment. Results show that explants remain viable up to one week without degenerative changes, show an increased enzyme production till day 4 of culture, and that oxytocin at a dose of 200 mIU/ml significantly increases (P<0.01) oxytocinase content of the cultivated placenta, without any effect on other parameters.
129. **Further Studies on the Antinociceptive Effect of Prostaglandin E**,

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Recent studies from this laboratory indicated that prostaglandin E, and \( F_2 \), had antinociceptive affect in rats after i. p. administration. Since the dose of PGE, employed was 2.0 mg/kg. it was thought worthwhile to confirm the effect by employing smaller doses and by direct intracerebroventricular administration. A dose response study with PGE, indicated that a dose of \( 5 \mu g/rat \) I. C. V. was sufficient to produce significant antinociceptive effect. With 20 \( \mu g/rat \) catatonia was observed in some rats and hence higher doses ware not tried. In order to elucidate the possible role of serotonin in PGE, antinociceptive effect, 5, 6-dihydroxytryptamine was used as a pharmacological tool to produced selective degeneration of serotonergic neurones. This pretreatment produced marked inhibition of PGE, antinociception. The role of prostaglandins in morphine analgesia was also investigated by using prostaglandin synthesis inhibitors. Indomethacin, diclofenac sodium, mefanamic acid, ibufen and paracetamol significantly inhibited morphine analgesia without affecting PGE, antinociception. The results of the present study, along with those reported earlier from this laboratory, confirm the antinociceptive effect of PGE, and also substantiate the involvement of serotonin and prostaglandins in morphine analgesia.

130. **Prostaglandin \( E_1 \) Induced Potentiation of Anticonvulsant Effect of Phenobarbitone and Inhibition of Pentylenetetrazol Convulsions in Rat : Role of Serotonin**

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In earlier communications from this laboratory we had shown that some central effects of prostaglandin \( E_1 \) \( (PGE_1) \) were mediated through serotonin. Subsequently
We also demonstrated that PGE₁, in the dose end route of administration used, significantly increased turnover of brain serotonin. In the present study the role of serotonin was investigated in PGE₁ induced potentiation of anticonvulsant effect of phenobarbitone (maximal electroshock induced hind limb extensor response) and inhibition of pentyleneterezol (PTZ) induced clonic convulsions in rat. Pharmacological agents known to inhibit synthesis, storage, receptor activity of serotonin or produce selective degeneration of serotonergic neurones, significantly inhibited PGE₁ induced potentiation of phenobarbitone and inhibition of PTZ convulsions. The results will be discussed.

131. Neuromuscular Blocking Activity of 3, 8-dimethylamino-6-phenylphenanthridine methiodide

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3, 8-Dimethylamino-6-phenyl phenanthridine methiodide was found to produce death of various animals in very small doses (LD₅₀ in mice 2.5 mg/kg i. p.). The death was preceded by muscular twitches and anoxic convulsions. The compound was, therefore, tested for its effect on neuromuscular conduction in cat (in vivo) and frog (in vitro). In eneesthetized cat sciatic nerve-anterior tibialis muscle preparation it showed a dose-dependent (0.025-0.1 mg/kg i. v.) neuromuscular blocking activity. The onset was immediate and the effect lasted for 30-60 min. The neuromuscular blockade of the compound was not modified by neostigmine and the tetanic stimulus was well sustained. In chronically denervated muscle of cat, the compound at a similar dose showed a sustained contracture when the muscle was stimulated directly. The effect of the compound simulated that of succinylcholine (0.05-0.1 mg/kg i. v.) in the above preparations. In isolated frog rectus abdominis muscle the compound produced contraction which could only partially be blocked by atropine but was completely abolished by tubocurarine. In doses producing complete blockade of neuromuscular transmission, it did not produce any fall in blood pressure or depression in respiration. On the other hand, in most of the experiments it increased the blood pressure and respiration. The compound did not alter the responses to adrenaline, acetylcholine, histamine on blood pressure and also it did not effect the ganglionic transmission as observed by preganglionic nerve stimulation to produce contraction of the nictitating membreton of cats. When an intravenous dose of 1.5 mg/kg was administered, the cat died due to cardiac failure.
132. **Role of Brain Monoamines in Pentylenetetrazol Convulsions in Albino Rat**

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The role of brain monoamines in pentylenetetrazol (PTZ) induced clonic convulsions was investigated in albino rat, by using pharmacological agents with well documented effects on brain monoamine turnover and receptor activity. Pharmacological agents increasing turnover of brain serotonin and noradrenaline significantly inhibited PTZ convulsions, whereas increase in dopamine concentrations did not. Decrease in brain serotonin and noradrenaline, by use of synthesis inhibitors and depletors significantly potentiated PTZ convulsions. Serotonin and noradrenaline, but not dopamine, receptor antagonists also potentiated PTZ convulsions. The results suggest that serotonin and noradrenaline are involved in PTZ convulsions in rat.

133. **Influence of Environmental Temperature on Pentobarbitone-Hypnosis in Male Rats**

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The hypnotic action of barbiturates is greatly influenced by the atmospheric temperature. Thus far, it has been generally considered, and some experiments have also proved, that animals sleep for a longer period at lower room temperature than at higher ones. However, during the pharmacological screening of certain drugs, it was observed in our laboratories that the control group of animals slept for longer periods in summer months than in winter. This finding prompted us to conduct systematic study on the duration of pentobarbitone-induced sleep in rats at various north-Indian atmospheric temperatures. Pentobarbitone sodium (40 mg/kg) was injected intraperitoneally to adult male albino rats at (±1) 15, 18, 21, 24, 27, 30, 33 and 36°C room temperatures. The respective dates when these temperatures existed (around 11 A.M.) at Izatnagar were December 15, January 30, February 28, March 22, April 3, July 31 and May 1, 1975. Ten rats were taken in each group. Statistical analysis was done by applying Duncan’s multiple regression test at 1 percent level of significance. The duration of sleep was significantly longer at 33 and 36°C than at the remaining temperatures. The animals at 21 and 15° slept for significantly shorter period than at 30°C. The duration of sleep at 27, 24 and 18° was not significant than at 30, 21 and 15°. The results would be discussed in the light of these findings,
134. **Neuromuscular Blocking Activity of a New Synthetic Basic Anilide vs Compared to Lignocaine**

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Local anaesthetics, procaine & lignocaine have been known to produce neuromuscular blockade. The compound under study (EA-7) is a synthetic basic anilide chemically related to lignocaine and has already been reported to possess significant local anesthetic activity. The antispasmodic activity of EA-7 has been demonstrated and found more potent than lignocaine in this respect. The present study envisages our findings on its neuromuscular blocking activity as compared to lignocaine. The drug (EA-7) was tested for its neuromuscular blocking property employing skeletal muscle nerve preparation viz. phrenic nerve diaphragm of rat and against acetylcholine induced contractions of the frog rectus abduminis muscle. It was found to be more potent than lignocaine against acetylcholine induced contractions of frog rectus. On phrenic nerve diaphragm its effect was comparable to that of lignocaine in blocking the neuromuscular junction. Neostigmine did not counteract the block produced by these compounds. However, the muscle responded to direct stimulation. The results shall be presented and discussed.

135. **A New Method to Assess Anticonvulsant Activity**

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Intraperitoneal administration of Z-methyl, 6-bromo-3N’-(Aminopropyl cyclohexyl)-4-quinazolone hydrochloride in albino rats produces convulsions in a dose of 80 mg/kg without any mortality for 24 hours. The convulsions were consistent and clonic in nature. They appear in 10-15 minutes at the rate of 30-40 per hour persisting for 3 hours. Each convulsion lasted for 60-70 seconds. Amongst the various drugs tested dilantin sodium (30 mg/kg), methaqualone (1 O-30 mg/kg), phenobarbitone (60 mg/kg), diazepam (5 mg/kg), carbamazeptepine (80 mg/kg), haloperidol (2 mg/kg), acetazolamide (80 mg/kg), chlorpromazine (1 mg/kg), myoline (400 mg/kg), ethasuxamide (400 mg/kg), pretreatment with ethasuxamide, methaqualone, phenobarbitone and diazepam prevented these convulsions. The remaining drugs showed no protection. Such a method may be of value in assessing anti-convulsant activity of drugs used in petit mal epilepsy. The present method seems to have definite advantage over the existing metrazol induced seizures method because of the lack of mortality and consistence of convulsions. The possible mechanism of these convulsions will be discussed.
136. Pharmacological Studies on 4′-Fluoro-3-(I-Piperidyl) Propiophenone-A Centrally Acting Muscle Relaxant

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4′-Fluoro-3-(1 -Piperidyl) propiophenone (compound CN) is the most active centrally acting skeletal muscle relaxant in a series of propiophenone compounds investigated. Compound CN showed the typical gross effects of a central muscle relaxant in mice and rabbits. It antagonised the tonic convulsions by pentylenetetrazol, strychnine and supramaximal electroshock and tremorine-induced tremor, but failed to inhibit the clonic convulsions by pentylenetetrazol in mouse. It showed a dose-dependent (1.25-50 mg/kg i.v.) spinal and supraspinal polysynaptic somatic reflex blocking activity without inhibiting the monosynaptic reflex or neuromuscular conduction in anaesthetized cat. It also counteracted the decerebrate rigidity. Quantitatively CN was found to be about four times more potent than mephenesin with the additional advantage of being longer acting and devoid of any haemolytic activity. It produced a dose-dependent (2.5-10 mg/kg i.v.) hypotension in anaesthetized cat, which was more pronounced on intracerebroventricular administration. The responses of adrenaline, tyramine and histamine (most effectively) on blood pressure were reduced. It also exhibited anti-histaminic activity (H1) in guinea-pig ileum (in vitro) and bronchial musculature (in vivo). The compound was devoid of any effect on myocardium in vivo but on the isolated guinea-pig atrium a depressant effect was seen with very high concentration (3 x 10^{-5} g/ml).

137. Effects of Different Pretraatments on Amphetamine Aggregation Toxicity

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A large amount of work has been carried out to elucidate the mechanisms involved in amphetamine aggregation toxicity. We used the animals pretreated with either of the four agents viz. phenobarbitone sodium, SKF 525 A, d-amphetamine sulfate and piribedil. The first two were used to alter amphetamine metabolism while the latter two were supposed to interfere with catecholaminergic mechanisms. Phenobarbitone sodium and d-amphetamine sulfate afforded the protection whereas SKF 525-A and piribedil did not do so. The results obtained were in exact accordance with the theoretical expectations. The details of the findings will be discussed.
138. Observations on the Mechanism of Audiogenic Seizures

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Audiogenic seizures, a type of cerebral dysrhythmia has been considered to be due to combination of three factors—(1) Predisposition either hereditary or constitutional. (2) Epileptogenic neuronal abnormality. (3) Biochemical or electrical change playing on these abnormal factors. The more the one is present, less the others are needed. Many strains of mice normally used in our laboratories are refractory to the audiogenic stimuli in producing typical audiogenic seizures. Using large number of drugs acting directly on neurones at different levels and by using a series of drugs modifying the concentrations of neurotransmitters in C. N. S. as well as intracerebro-ventricular injections of drugs, an attempt has been made to convert audiogenic negative mice into audiogenically positive animals. The results will be discussed.

139. Effect of Diazepam on Anticonvulsant Action of Phenobarbitone. Diphenylhydantoic and Carbemazepine

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Phenobarbitone or diphenylhydantoin used singly is often found to be inadequate for complete control of epileptic seizures. Diazepam is not in use alone or in combination as an established therapy of epilepsy. The effect of addition of a small dose of diazepam on anticonvulsant property of phenobarbitone, diphenylhydantoin and carbemazepine has been determined by employing the technique of maximal electroshock seizures in albino rats. Addition of diazepam increased anticonvulsant response of phenobarbitone and diphenylhydantoin by 38 per cent and that of carbemazepine by 8 percent. Chronic administration of diazepam with carbemazepine increased the anticonvulsant response of carbemazepine from 50 per cent to 92.37 per cent.

140 Convulsant Activity of a new Hormone Derivative

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In a series of chromene derivatives screened for their activity on central nervous system compound \( N-(\Delta^3\text{-chromene-3-carbonyl})-4\text{-imino-3, 4-dihydropyridine} \)
(69/224) was found to possess a potent convulsant activity. The LD50 of this compound was found to be 35 mg/kg i.p. and 55 mg/kg p.o. in mice. The animals showed tonic convulsions similar to strychnine which was followed by death. Various central nervous system depressants were tested for their ability to antagonise the convulsions. Mephenesin was found to afford maximum protection against the convulsions and death by the compound in mice. Compound 69/224 augmented the various polysynaptic (spinal and supraspinal) and monosynaptic (spinal) somatic reflexes in chloralosed cats. At doses of 0.1-0.3 mg/kg i.v., the Polysynaptic flexor, crossed extensor and linguomandibular reflexes were facilitated by 50% but a higher dose was required for facilitation of the monosynaptic reflex. The only other pharmacological effects of this compound were mild pressor (16-26 mm Hg) effect lasting for 5-15 minutes, and an increase in respiration.

141. Synergism of Morphine Analgesia in Mice

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Analgesia was tested in mice and the ED50 of morphine, some tranquillisers and antidepressants, ephedrine and atropine with 95% fiducial limits were determined. The ED50 values (mg/kg) were as follows: morphine 3.1, chlorpromazine 8.7, triflupromazine 5.96, prochlorperazine 8.14, haloperidol 2.0, diazepam 4.06 and ephedrine 8.70. Atropine was ineffective as analgesic at 5 mg/kg and both imipramine and nialamide at 40 mg/kg. Pretreatment with each of the above tranquillisers or ephedrine caused synergism of morphine analgesia and the fractions of the independently effective ED50 of the drugs producing synergism were as follows: chlorpromazine 0.27, morphine 0.376, triflupromazine 0.49, morphine 0.40, prochlorperazine 0.35, morphine 0.43, haloperidol 0.55, morphine 0.44, diazepam 0.57, morphine 0.37, ephedrine 0.85, morphine 0.38. The possible mechanism of the synergism of morphine analgesia will be discussed.

142. Comparative Experimental Evaluation of few Analgesics with and without Amphetamine

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Comparative analgesic activity of dextropropoxyphene, pethidine and analgin was assessed individually and in combination with amphetamine in rat by radiant heat
and in mice by p-benzoquinone induced writhing syndrome method. Amphetamine per se exerted profound analgesia and an optimal dose that increased the threshold reaction time of rat tail up to 100% was found to be 5.75 mg/kg. The peak analgesic effect was seen at second hour after oral administration. However amphetamine, when combined with other analgesics in minimal subthreshold doses (1.25 mg/kg), potentiated significantly the analgesic activity of dextropropoxyphene (P<0.01) and pethidine (P<0.05) but antagonised the activity of that of analgin. The same results were seen by using writhing syndrome in which ED50 was determined and compared. Oncomparation of equianalgesic doses and ED50 ratios, it was found that the analgesic efficacy was highest in amphetamine and lowest in analgin in the order i.e. Amphetamine>Dextropropoxyphene>Pethidine>Analgin. Results indicate that amphetamine will add to the therapeutic advantage when combined with dextropropoxyphene.

143. Modification of the Pyretogenic Effect of Drugs by Electroconvulsions

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Reserpine induced adynamia and ptosis are enhanced and methamphetamine induced hyperactivity is reduced in rats subjected to electro-convulsive shock (ECS) delivered once daily for seven days. In rabbits similarly exposed to electro-convulsions, the hypothermic effect of reserpine and chlorpromazine and the antipyretic effect of salicylates against T. A. B. pyrexia are reduced. It was decided to study in detail the interactions between electroconvulsions and CNS active drugs on body temperature. The study was carried out in rabbits of either sex weighing between 1.50 kg and 2.00 kg at 30°C. The rabbits were given ECS (with the help of an electroconvulsometer) once a day for seven days. On the day of the experiment their rectal temperature was recorded by telethermometer for 5 hours after the administration of the drug under study. The drugs used were L. S. D-25, J. B-516, reserpine, T. A. B. vaccine and nor-adrenaline. LSD-25 and J. B-516 were injected into the marginal ear vein, T. A. B. vaccine and reserpine were given by intraperitoneal injection and nor-adrenaline was administered by intracerebroventricular route. ECS exposure per se did not produce any significant change in body temperature but enhanced the pyretogenic effect of L. S. D-25 and T. A. B. The pyrexia due to a combination of J. B-516 and reserpine was also more in ECS treated animals. There was no significant difference in the pyrexia induced by icv nor-adrenaline in normal and treated animals. It seems that increased permeability of drugs into C. N. S. may be responsible for the observed effects.
144. **Anticonvulsant Action and Toxicity Study of Carbamazepine**

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This study has been undertaken on albino rats to evaluate the anticonvulsant potency and toxicity of carbamazepine. Two groups of rats, 10 rats in each group, weighing between 150 to 250 g were taken for the purpose of this study. The experiments were carried out by inducing convolution on experimental animals (a) Electrically in a convulsiometer and (b) Chemically by administering metrazol. The anticonvulsant efficacy of carbamazepine have been found out at more than one dose levels. The anticonvulsant effects and toxicity have been compared with phenobarbitone taking it as reference standard drug.

145. **Experimental Studies on the Role of Biogenic Amine in Convulsive Seizures**

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The effect of pretreatment with agents altering the brain concentration of catecholamine, 5-HT and histamine was investigated on experimentally induced seizures in rats in 3 phases. In the first phase the different groups of rats were pretreated with biogenic altering agents and after 24 hours given pentylentetrazol 70 mg/kg intraperitoneally. Percentage of seizures with different pretreatments was: reserpine 100%, nialamide 80%, alphamethyl dopa 10%, 5-HTP 0%, alpha MMT 0%. In the second phase different groups of rats were pretreated with 5-HTP 50 mg/kg and PCPA 300 mg/kg respectively and after a suitable interval subjected to electroshock, amphetamine and thiosemicarbazide induced seizures. Whereas 5-HTP increased the threshold for minimal electroshock seizures and protected rats against chemoshock seizures, PCPA pretreatment reduced the former and exacerbated the latter. In the third phase the effect of histamine 1 mg/kg injected intracerebroventricularly (IVT) and pretreatment with L-histidine 1 g/kg intraperitoneally (I.P.) was studied on the electroshock and chemoshock seizures in rats. Both the drugs reduced markedly the threshold for m.e.s. and chemoshock seizures. These studies indicate that an increase in the brain 5-HT level protected against while increase in the catecholamines and histamine level enhanced the susceptibility to seizures.
146. Influence of Sulfonamides on the Anticonvulsant Effect of Phenyoit in Rats
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Since a major portion of an administered dose of phenytoin after absorption is bound to plasma protein-mainly albumin, an interaction of it may occur with a concomitantly administered drug or drugs having varying binding affinity to this plasma protein as a result of displacement of one of the two from their binding site. Which of the two will be affected would depend upon the dose of two drugs, their relative binding affinity to plasma proteins and the plasma protein status of the subject. In the present study influence of some sulfonsmides (sulfadimethoxine, sulfaphenazole, sulfadiazine, sulfapyridine and sulfacetamide) having different binding capacity to plasma albumin has been investigated on the maximum electroshock seizure pattern produced by phenytoin in rats. Various sulfonamides which have no anticonvulsant effect of their own, were found to potentiate the effect of a subanticonvulsant dose of phenytoin. However, no correlation was observed between the degree of potentiation of the anticonvulsant effect of phenytoin and the protein binding capacity of a sulfonamide. In the light of further observations, the role of protein binding in this interaction will be discussed.

147. Marina Organisms as a Source of Substance Possessing Pharmacological Activities
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The chemical contents of several hundreds of marine organisms were examined for various pharmacologic activities in an attempt to explore the potential of sea as a source for drugs. A pharmacologic profile of some of the extracts of marine organisms possessing activity on the central nervous system has been reported. Of the organism studied, the extracts of Aplysia dactylomela, Sphanciospongia vesparia, Stypodium zonale, Actinopyga agassizi which showed significant CNS depressant activity were subjected to chemical fractionation in order to isolate and identify the chemical moiety responsible for their activity. The follow up study indicated a potent hypnotic property in the fractions of A. dactylomela which led to the isolation of dactylyne. A detailed pharmacologic study on this compound was undertaken.
148. The Case of Transmitter Release by Oxotremorine at a Central and Peripheral Cholinergic Synapse

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The capacity of oxotremorine to mimic many features of Parkinson’s disease has convinced a number of investigators of its potential value for providing insight into the basic mechanism of extrapyramidal tremor and rigidity. We earlier demonstrated, for the first time, employing a nerve muscle preparation that oxotremorine at small doses could produce spontaneous fasciculations of skeletal muscle and a paralytic effect at higher concentrations. A presynaptic effect of oxotremorine was also postulated. The possibility of transmitter release by oxotremorine at the peripheral cholinergic synapse of neuromuscular junction as well as at the central cholinergic synapse of motor axon collaterals to Renshaw cells was examined in the present study. Both direct and indirect evidence will be presented for enhanced release of the transmitter upon administration of the Parkinsonimimetic agent, oxotremorine.

149. Effect of Centbutindole on the Neuronal Activity in the Caudate Nucleus

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Centbutindole a new majortranquilliser has been studied for its affects on the activity of neurones in the caudate nucleus of rat on intravenous administration. Urethane anaesthetised rats weighing between 250-350 g were used. Standard single unit recording technique was employed. After opening the skull and reflection of the duramater, a single barrel microelectrode was lowered vertically into the caudate nucleus stereotaxically (A 8.5, L 2.5, H 2.5). The firing rate of a group of neurones was recorded before and 30 minutes and 3 hours after the intravenous administration of the compound. Control saline experiments were also run concurrently. Centbutindole produced a significant increase in the firing rate (p<0.001) at 30 minutes in a dose of 2 mg/kg, but at 3 hours the effect was over. A dose of 5 mg/kg produced a significant increase in the firing rate both at 30 minutes and 3 hours (p <0.001). Chlorpromazine and haloperidol also produced similar effects. In view of the known inhibitory effect of dopamine on these neurones, the increase in firing rate by neuroleptics is possibly related to their dopamine recepter blocking activity.
150. Evidence for Stereospecific Nature of Neuroleptic Action of Centbutindole

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Centbutindole is a new potent haloperidol type neuroleptic. The clinical efficacy as well as dopamine receptor blockade by butyrophenones is stereospecific. Centbutindole has an asymmetric centre and its d- and l-isomers could, therefore, be prepared. The three compounds have been quantitatively evaluated for CNS effects, acute toxicity and anti-inflammatory activity. The CNS activity was assessed by effect on spontaneous motor activity (mice), secondary conditioned, conditioned and unconditioned avoidance responses (rats), antagonism of amphetamine induced stereotypy (guinea-pigs) and hyperactivity (mice), and antagonism of apomorphine induced stereotypy (guinea-pigs, pigeons) and emesis (dogs). The l-isomer was uniformly more active and in most tests it had twice the potency of diracemate. The d-isomer had little activity and in certain tests appeared to antagonise the activity of l-isomer. The anti-inflammatory activity was also stereospecific but the acute toxicity was not. A second set of optical isomers obtained by sodium borohydride reduction of the 3 compounds was also tested for some CNS effects and essentially similar findings were obtained. Molecular models of the two sets of isomers suggest that only the l-isomer resembles the configuration in which dopamine probably acts in CNS.

151. Effects of Different Anticholinergic Drugs on Amphetamine Aggregation Toxicity

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Different factors have been implicated in causation of amphetamine aggregation toxicity. Increased body temperature has been said to be one of the factors involved. Amphetamine induced hyperthermia can also be modified by some centrally acting anticholinergic drugs, and this has stimulated us to undertake the present work. In the present study we have used the two natural alkaloids and some synthetic atropine substitutes. From the results it appears that the anticholinergics do modify the amphetamine aggregation toxicity. The details of the results obtained will be discussed.
152. Modification by 6-Hydroxydopamine of Pyrexia Induced by Some Centrally Acting Agents in Rabbits
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6-Hydroxydopamine (6-OHDA) is known to cause release of noradrenaline from and to cause degeneration of adrenergic nerve terminals. This property has been made use of in analysing the role of presynaptic adrenergic influences in the pyrexia induced by several agents by their central action in rabbits. Noradrenaline (NA), dopamine (DA), PGE,
LSD and TAB vaccine, when administered into lateral cerebral ventricle of rabbit in small doses, induce pyrexia. After central 6-OHDA pretreatment the pyrexia induced by NA remained unaltered while the pyretic responses of PGE,
LSD and TAB vaccine were attenuated. The DA response was potentiated but it could be significantly reduced by dopamine receptor blocking agent haloperidol in 6-OHDA pretreated rabbits. The results obtained in this study indicate the essential role of adrenergic fibres in the mediation of pyretic response of the above mentioned agents except DA. It appears that in the case of DA perhaps only a part of the effect is due to its conversion to NA and that there is a separate dopaminergic mechanism also involved in its pyretic response.

153. Pharmacological Studies with an extract prepared from the Liver of Poisonous Fish
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The ingestion of the fish, known as Bang fish in Bengal (T. Patoca), is followed by toxic manifestations. This communication describes some pharmacological action of an extract prepared from the liver of this species by solvent extract, dialysis and drying of dialysate in partial vacuum. Liver extract (LE) resulted in quietening and paralysis of limbs in mice. LE was found to have local anaesthetic activity on infiltration, as tested with guinea pig wheal method. No local anaesthesia ensued with surface application. On intrathecal administration to rabbits, limb paralysis ensued and urethral reflex disappeared. No analgesic activity could be demonstrated. Muscle relaxant activity was found with LE in rat phrenic nerve diaphragm preparation. At low concentration LE potentiated the neuromuscular relaxant activity of a-TC. LE when painted in rat sciatic nerve, impulse conduction is impaired in response to electrical stimuli.
154. **Release of Noradrenaline into Perfused Cerebral Ventricles in Unanaesthetized Dogs**

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The cerebral ventricles were perfused in unanaesthetized dogs from lateral ventricles to cervical subarachnoid space with sterile artificial c.s.f. at 0.3 ml/min. The effluent was assayed for noradrenaline with the help of Spectrophotofluorometer. The noradrenaline output in the samples collected every 10 minutes is expressed in nanograms per minute. In the wakeful state, when the animals’ behaviour was normal, the output was about 20-40 ng/min noradrenaline. When the animal was restless the output was 30-50 ng/min. When there was infection of the meninges the output rose to 240-260 ng/min. The first sample collected on perfusion was containing more noradrenaline.

155. **Anticonvulsant and Succinate Dehydrogenase Inhibitory Activity of some Newer Thiobarbiturates**

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Several barbiturates have been reported to exhibit anticonvulsant and succinate dehydrogenase inhibitory activity. In the present study some newer 1-aryl-3-cyclohexyl thiobarbiturates were synthesized and investigated for their ability to inhibit succinate dehydrogenase (SDH) activity of rat brain homogenate. All compounds exhibited a concentration dependent inhibition of enzyme. The degree of enzyme inhibition was also evaluated on the basis of their \( I_{50} \) values. Among these compounds, 1-(2-ethoxyphenyl)-3-cyclohexyl thiobarbiturate was found to be most potent inhibitor of succinate dehydrogenase. Kinetic study carried out with 1-(2-ethoxyphenyl)-3-cyclohexyl thiobarbiturate revealed a competitive nature of inhibition. Anticonvulsant activity of these compounds was determined against pentylenetetrazol-induced seizures which ranged from 10 to 60% at dose of 100 mg/kg. All compounds were also investigated for their partition coefficient values to find out lipophilic nature of these thiobarbiturates. Present investigation was made in an attempt to investigate the effect of these compounds on complex II of Electron Transport Chain (E. T. C.). The inhibitory action of these thiobarbiturates on complex II of E. T. C. can be ascribed to be due to the action of these compounds on succinate dehydrogenase, a constituent of complex II. However, these studies were unable to provide a definite correlation between anticonvulsant activity, the ability to inhibit SDH activity of rat brain homogenate and lipophilic nature of these substituted thiobarbiturates.
156. Effect of Intracerebroventricular Administration of Ouabain on Morphine Analgesia in Mice

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Effect of Intracerebroventricularly administered ouabain on morphine analgesia is studied with the help of hot wire technique. Ouabain (0.3 μg) is found to antagonise the morphine induced analgesia; ED50 of morphine was increased from 12.02 mg/kg to 16.22 mg/kg in ouabain pretreated mice. Ouabain 0.3 μg produced reserpine like sedative effect. This effect in mice is associated with selective increase in dopamine level in brain. Increase in dopamine levels in brain after ouabain may be responsible for antagonism of analgesic effect of morphine. This is being further confirmed by studying the effect of L-3, 4-dihydroxyphenylalanine (L-dopa) and haloperidol on above interaction. The results will be discussed.

157. Experimental Evaluation of Antiemetic Activity of Centbutindole: A New Neuroleptic Agent

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Centbutindol, a new major tranquiliser, was evaluated for its antiemetic activity in dogs and was compared with haloperidol and chlorpromazine against apomorphine, morphine, ouabain, protoveratrine, emetine and copper sulphate (oral) induced emesis. The compounds were administered 30 min prior to the administration of a predetermined 100% effective challenging dose of the emetic agents. Centbutindole afforded protection against emesis induced by all the emetic agents. The maximum activity was seen against apomorphine induced emesis (ED50, 11.7 μg/kg) and minimum against protoveratrine (ED50 1.12 mg/kg). Haloperidol had a similar pattern of efficacy and was somewhat more potent, the potency ratio varying 1 to 2.5 times against different emetic agents. It appeared that centbutindole like haloperidol was acting on CTZ in low doses and in higher doses the action extends on vomiting centre. Chlorpromazine was much less active and devoid of action on the vomiting centre. Centbutindole was quite effective by oral route and the oral absorption was comparable to haloperidol. Chlorpromazine is much less absorbed. The antiemetic activity of centbutindole persists for over 32 hours even following i.v. administration. Centbutindole is thus a potent, versatile and long acting antiemetic agent meriting clinical investigation.
158. Paracetamol Toxicity and Protective Effect of Indigenous Drugs

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Large doses of paracetamol have been reported to produce toxic effects on liver in human patients. In a study on rats it is seen that paracetamol in doses of 1 gm/kg causes loss in weight and mortality of 26% in group of rats after 15 days treatment. Simultaneous administration of Liv. 52 prevents the weight loss and mortality. The antipyretic effect of paracetamol (150 mg/kg) studied in rabbits after i. v. TAB was unaffected by Liv. 52. Paracetamol administered to rats, in whom formalin arthritis was induced, seemed to cause increase in inflammatory reaction. Simultaneous administration of compound 1830 which is closely related to Liv. 52 prevents this increased inflammatory activity. It appears that Liv. 52 protects rats against liver damage caused by large doses of paracetamol but does not interfere with the therapeutic antipyretic activity as tested in rabbits. The cause of increased inflammatory reaction caused by paracetamol is not known but it is possible that liver damage caused by paracetamol may indirectly cause such an effect in which case its antagonism by compound 1830 may be another evidence of protection from liver damage.

159. Brain Monoamine Metabolites in Iatrogenic Parkinsonism

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Homovanillic acid and 5-hydroxy-indole acetic acid levels were estimated in lumbar CSF of 10 cases of chlorpromazine induced Parkinsonism. These metabolites reflect the concentrations of dopamine and serotonin in human brain. 40 cases of schizophrenia were put on chlorpromazine therapy, out of them 10 developed extrapyramidal syndrome. The initial levels of homovanillic acid (HVA) and 5-hydroxy-indole-acetic acid (5-HIAA) in cerebrospinal fluid of these 10 patients were compared with the levels observed after development of extrapyramidal syndrome. Mean HVA concentration in CSF after development of syndrome ($59.44 \pm 15.98$ ng/ml) was significantly higher when compared to that before development of syndrome ($28.84 \pm 6.542$ ng/ml). On the other hand no significant change was observed in 5-HIAA values. The mechanism by which chlorpromazine increases the formation of HVA in brain is not known. Chlorpromazine possibly enhances the formation of dopamine through a feedback mechanism resulting from blockade of the dopamine receptors. The results also show that serotonin does not play a role in iatrogenic Parkinsonism.
160. Hypothermia-Molecular Conformation and Tranquillisation: A Possible Triangle in Phanothiazina Mode of Action

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It has been postulated that prior to eliciting tranquillisation, the phenothiazine tranquillisers probably assume a 3-dimensional conformation at the receptor site. Further, it has been proved that at lower temperatures (below 32°C), the side chain of phenothiazine tranquilliser does fold over the plane of the phenothiazine ring structure to assume a three-dimensional character. Since phenothiazines also cause hypothermia, it was contemplated from the above reports that the fall in body temperature may not be a mere side effect but a prerequisite for 3-dimensional conformation to occur. Might be, it is serving as an important step in a ladder prior to tranquillisation. Hence, the tranquillisating effects of chlorpromazine at 20°C, 28°C, and 38°C±1°C have been studied and compared using a battery of parameters to find out if an essential correlation exists in between Hypothermia-Molecular conformation and Tranquillisation produced by phenothiazina drugs. The results will be discussed.

161. Modification of β-Phenylethylamine Induced Stereotyped Behaviour by Sax Steroids

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Amphetamine induces stereotype in animals and has been proposed as an experimental model for tardive dyskinesias. Behavioral effects of β-phenylethylamine (PEA) specifically stereotypy is similar to amphetamine and there is evidence that it acts through similar dopaminergic mechanisms. Moreover, PEA is an endogenous compound, hence it is more logical to use PEA-induced stereotypy as a model for tardive dyskinesias in understanding the neuro-physiological state of tardive dyskinesias. In the present study, the effect of sex steroids, viz., testosterone, progesterone and estrogen on PEA-induced stereotypy in mica was carried out. The stereotyped behavior (SB) consisted of sniffing, biting, licking and head movements was quantified for 60 minutes by two independent observers, 15 min after the PEA treatment. Both acute and chronic treatments of steroids decreased SB very significantly. At present the decrease of SB may be attributed to two possibilities, (1) enhancement of PEA metabolism by the steroids, and (2) the effect of the steroids might be mediated through central neurotransmitters.
162. Possible Involvement of 5-Hydroxytryptamine and Cyclic-AMP in Tolerance to Tremorine Analgesia in Mice

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The phenomenon of tolerance to the analgesia by tremorine in mice was studied by the hot-plate and tail-clip methods. Reduction of 5-HT levels in brain by parachlorophenylalanine pretreatment decreased the ED50 of tremorine analgesia in tremorine tolerant mice. Pretreatment with 5-hydroxytryptophan (5-HT precursor) I-dopa (catecholamine precursor) or a-methyl-para-tyrosine (catecholamine depletor) did not influence the analgesic response to tremorine in tremorine-tolerant animals. However, theophylline pretreatment, to inhibit brain phosphodiesterase and thus raise CAMP levels, was found to increase the ED50 of tremorine in tolerance mice, i.e. increased tolerance analgesia. It is concluded that brain 5-HT and cAMP are both involved in the phenomenon, the former responsible for maintaining the tolerant state and the latter increasing the tolerance to tremorins analgesia, whereas dopamine and noradrenaline are not involved.

163. Evidence of Abstinence Syndrome in Cannabis Treated Albino Rats

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Albino rats of either sex were fed petroleum ether extract of Cannabis indica ad libidum mixed in a special semifluid diet in a series of experiments for three weeks. A record of body weight, rectal temperature and daily intake of diet was observed as compared to control groups. After 3rd week the rats stopped taking their feeds and then were subjected to audiogenic stimuli for 30 seconds every 24 hour. 20% animals showed convulsions within a week of abstinence. In another series of experiments rats were treated orally with fixed doses for 3 weeks and then subjected to audiogenic stimuli as above. 30% rats showed convulsions after first week of abstinence. These results suggest that Cannabis indica produces abstinence symptoms after chronic administration.
164. Effect of Central Synaptic DA Level Increasing Agents Alone and in Combination with Apomorphine in Open Field Situation in Rats
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Effect of synaptic DA level increasing agents (Benztropine, amphetamine, and L-dopa) alone and in combination with apomorphine was investigated in Open Field situation in albino rats. Apomorphine alone significantly decreased the ambulation and rearing score. It also antagonised the effect of synaptic DA increasing agents. The effect of apomorphine is similar to clonidine which is a central presynaptic receptor simulating agent. The results will be discussed.

165. Involvement of Gamma-Amino Butyric Acid (GABA) in the Anti-convulsant Actions of Methaqualone
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Effect of methaqualone on isonicotinic acid hydrazide, 6-mercaptopropionic acid, picrotoxin and strychnine induced convulsion was carried out in mice and results are compared with diazepam. Methaqualone like diazepam was found to be a selective antagonist of isoniazid elicited convulsion and a much less effective inhibitor of strychnine convulsions. Methaqualone elicits muscle relaxant, sedative and anti-convulsant effects at different dose level i.e., low doses (non-sedative dose level) produces anticonvulsant and higher doses muscle relaxant and sedative effects. The ability of methaqualone is more to overcome the convulsion elicited by GABA deficiency or receptor blockade than glycine.

166. An Approach to the Mechanism of Apomorphine Induced Fighting in Rats
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Spontaneous aggression has been induced by apomorphine and L-dopa. The role of super-sensitivity of the post synaptic dopamine receptors in apomorphine induced fighting has been delineated. Reserpine, α-methyl-p-tyrosine, clonidine and 6-hydroxydopamine potentiated the spontaneous aggression, while, pimozide
haloperidol, benztropine, amantadine; d-amphetamine and imipramine have antagonised the apomorphine induced spontaneous aggression. Pretreatment with l-dopa has been found ineffective. It is suggested that apomorphine action on presynaptic dopamine receptors plays a critical role in inducing spontaneous aggression of paired albino rats.

167. Haloperidol : A Better Antagonist of LSD

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The antagonism of the effects of LSD by three agents namely chlordiazepoxide, chlorpromazine and haloperidol was studied using Open Field test technique in rat. Two types of stereotyped responses produced by LSD i.e. ambulation and rearing were observed. It was found that haloperidol completely blocked both the stereotyped responses caused by LSD, whereas chlorpromazine antagonized its effect only on ambulation. Chlordiazepoxide failed to antagonize either type of behavioral patterns of LSD. It is suggested that haloperidol is a more complete antagonist of LSD than the other two agents.

168. Pharmacologic Agents and Foot Shock-Induced Aggressive Behaviour of Albino Rats with Special Reference to Lithium

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Non-neurotoxic doses of chlorpromazine (CPZ, 0.5-2.5 mg/kg) and scopolamine (0.05-0.25mg/kg) produced decrease of foot shock-induced aggressive behaviour of albino rats at 0.5 to 8 hour post-drug intervals. LiCl (1.2 and 3 mEq/kg) inhibited the aggressive behaviour upto 24 hours. Diazepam (2.5 mg/kg) however, facilitated the fighting, jumping and vocalization between 0.5 to 4 hour post-drug period. d-Amphetamine sulphate (0.5-2.5 mg/kg) also enhanced the fighting behaviour. Foot shock-induced fighting behaviour has been compared with 'arousal' phenomenon. The facilitation of fighting behaviour by d-amphetamine and inhibition by CPZ may be related to the influences these drugs exert
on the ‘arousal’ phenomenon. The inhibitory action of central cholinolytic scopolamine corroborated the earlier studies. Disinhibition of the rat’s anxiety or fear by diazepam (2.5-5.0 mg/kg) may explain the facilitation of fighting behaviour. The antagonistic actions of LiCl against scopolamine-induced inhibition and d-amphetamine-induced facilitation of the aggressive behaviour (unlike other psychotropic drugs) has been suggested to be due to the possible role of LiCl in ‘normalizing’ induced disturbances of both central adrenergic and cholinergic mechanisms.

169. Role of Brain Monoamines in the Anticonvulsant Effect of Phenobarbitone and in Nialamide Induced Potentiation of Phenobarbitone in Albino Rat

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The role of brain monoamines in the anticonvulsant action of phenobarbitone against maximal electroshock induced seizures, was investigated in albino rats. In addition, the role of brain monoamines was also investigated in nialamide induced potentiation of a sub-anticonvulsant dose of phenobarbitone. The anticonvulsant action of phenobarbitone was significantly inhibited by drugs inhibiting the storage, synthesis and receptor action of brain serotonin and noradrenaline. In addition, drugs known to cause selective degeneration of serotonergic and noradrenergic central neurones, also produced marked inhibition of phenobarbitone effect. However, dopamine receptor antagonists had no effect. A sub-anticonvulsant dose of phenobarbitone was significantly potentiated by treatments known to increase brain turnover of serotonin and noradrenaline. Increase in levels of dopamine or pretreatment with dopamine receptor agonists had no significant potentiating effect. Reserpine induced antagonism of phenobarbitone was significantly reversed by pretreatments increasing brain turnover of serotonin and noradrenaline, but not by enhancing brain dopamine levels. Nisamide induced potentiation of phenobarbitone was inhibited by drugs known to lower turnover of brain serotonin or block serotonergic receptors. The results suggest that the anticonvulsant action of phenobarbitone is mediated via brain serotonin and noradrenaline but not dopamine. Nisamide induced potentiation of phenobarbitone, however, is serotonin dependent. The results will be discussed.
170. **Studies on the Behavioral Effects of Oral Contraceptive Drugs in Albino Rats and Mice**

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Oral contraceptive drugs (oestrogen, progestogen and combinations) have been incriminated for behavioral toxicities such as anxiety, tension, depression, sleep disturbances, fatigue and headache. Effects of single and repeated doses (mg/kg) of ethenylestradiol (OE) (rat 0.004; mice 0.002). allyl-estrenol (PG) (rat 0.02; mice 0.01) and lynoestrenol and ethenylestradiol (OP) (Noracyclin; rat 0.084; mice 0.042) were studied on spontaneous motor activity (SMA) and pentobarbitone-induced sleeping time (ST) in mice and gross behavior and septal lesion-induced hyper-excitability in albino rats. While significant decrease of SMA was observed after OE and PG (single doses) and OP (repeated doses), enhancement of ST occurred after repeated doses of OE and PG. These results suggest a possible effect of these drugs on the brain areas controlling motor activity and emotions. No significant change in the gross behavior of the rats were found during the present study. The inhibitory effect of repeated doses of the combination preparation on the septal lesion-induced hyper-excitability may be related to the role of oestrogen-progestogen in maintaining emotional equilibrium.

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### RESPIRATORY & EXCRETORY SYSTEM

171. **Role of β-Adrenergic Mechanism in Diuretic and Antidiuretic Actions of some Agents in Rats**

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Anti-diuretic action of β-adrenergic stimulant isoprenaline is well known. It has been reported in the literature that anti-diuretic action of vasopressin is mediated
through $\beta$-adrenergic receptors. Anti-diuretic action of isoprenaline has been attributed to endogenous ADH. However xanthine alkaloids namely caffeine end theophylline possessing diuretic activity inhibit enzyme phosphodiesterase and elevate the levels of cyclic AMP which is known to promote $\beta$-adrenergic activity. Thus there appears to be a common cellular mechanism for both diuretic and antidiuretic actions. The present study was carried out to investigate the role of $\beta$-adrenergic mechanism in actions of isoprenaline, ADH, caffeine and theophylline. Results will be discussed.

172. Diuretic Effect of Furosemide Metolazone Combination in Anaesthetised Dogs  
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Our clinical studies have demonstrated that furosemide-metolezone combination produces supra-additive diuretic effect in patients with hepatic cirrhosis or chronic renal failure. However it is difficult to attain supramaximal doses of furosemide in patients. The present study was therefore undertaken to study diuretic effect of submaximal and supramaximal doses of these drugs. Anaesthetized dog was used as experimental model. The results of these studies will be discussed.

173. Effect of Hypoxia on Lung P-V Characteristics in Food Deprived Rats  
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The hysteresis obtained in excised lungs on being inflated and deflated with air has been attributed to the pulmonary surfactant system. Food deprivation or diet rich in fats is likely to modify the turnover of lungs surfactants in animals. We have found that in lungs of rats deprived of food for 56 hours and then subjected to simulated hypoxia equivalent to 6100 m for 5 hours, consistently retained more air during deflation at low transpulmonary pressures. This is possibly, due to increased pulmonary surface tension due to combined effect of food deprivation end hypoxic hypoxia. It is likely that small airways, in such a conditions, close prematurely resulting in greater quantum of air being trapped in the alveoli.
174. **Effect of Acute and Chronic Pre-treatment of Chloroquine on the Hypnotic and Anti-Convulsive Activity of Methaqualone in Mice and Rats**

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The discovery of 2-methyl-1-3-tolyl-quinazoline (Methaqualone) is an important landmark in the field of synthetic non-barbiturate hypnotics. It also possesses anticonvulsant properties. Chloroquine is found to promote rapid metabolism of pentobarbitone and it is possible that it can induce the metabolism of other drugs too. As an anti-malarial drug it is commonly used by the people, thus it was thought interesting to study its effect (after acute and chronic pre-treatment) on the hypnotic and anticonvulsant activities of methaqualone in mice and rats. The results will be discussed.

175. **Antagonism of Cholera Toxin induced Rat-paw Oedema by Drugs**

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Rat hind paw oedema was produced by lyophilised preparation of crude cholera exotoxin obtained by inoculation of classic Vibrio 5698 Haffkine Strain in a medium containing 2% Bactopeptone in distilled water. Various drugs were tried for their possible antagonistic effects against the rat hind paw oedema caused by cholera exotoxin. The drugs tried were Phenylbutazone, Prednisolone, Nor-adrenaline, Alpha-adrenergic blocking agents, Antihistaminics. Aminophyllin, Prostaglandin E₁, Prostaglandin F₂α etc. The course and nature of the paw oedema produced by cholera exotoxin has also been compared with the oedema produced with the standard phlogistic agent carrageenin.
176. Subacute Toxicity Studies of O-ethyl-S. S-diphenyl Phosphorodithioate in Buffalo Calves

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O-ethyl-S, S-diphenyl phosphorodithioate (Hinosan, Bayer 78418) an organophosphosphate anti-fungal and insecticidal compound, has a specific action against Pyricularia oryze, the causal organism of blast disease of paddy. With high yielding varieties of paddy becoming popular in our country the use of Hinosan has increased many times and poses a health hazard to livestock. The present investigation was undertaken to study the effect of oral administration of repeated doses of this compound on various blood enzymes and other biochemical parameters in buffalo calves. Hinosan in doses of 4 and 8 mg/kg was administered (P.O.) daily for 28 days to buffalo calves and its effect on whole blood choline-sterase activity, SGO-T, SGP-T, serum alkaline phosphatase, blood glucose blood lactic acid, total serum cholesterol and serum creatinine was studied. Animals fed with 4 mg/kg dose of Hinosan daily upto 28 days showed no toxic manifestations. However, all the animals dosed with higher dose (8 mg/kg/day) died between 13-17 days after its administration. The whole blood ChE activity was inhibited at both dose levels and maximum inhibition was recorded after 12th and 28th day of its administration with 8 and 4 mg/kg doses, respectively. An increase in SGO-T level was found in all Hinosan treated animals and the rise was more marked at the higher dose. No marked change in other biochemical parameters was observed during the course of toxicity study.

177. Genetic Toxicological Evaluation of Diazepam (Valium) in Wistar Rats

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Diazepam (Valium) is one of the most commonly used tranquillizers and a skeletal muscle relaxant. It it generally considered to be free from any teratogenic effects. There are, however, studies of in vitro chromosome damaging effects of diazepam in cell cultures. We have previously reported lack of Valium to induce any in vivo chromosomal damage in the somatic tissue. The present investigation was undertaken to examine, the in vivo mutagenic effects, if any, of Valium in the germ cells since the literature survey failed to reveal any such report. Male rats were randomly
assigned to four groups and given saline alone, or 5 or 10 mg/kg of Valium in saline or exposed to 200R x-rays. All the animals were weekly paired with untreated virgin females sequentially for eight weeks. Examination of the females mated with Valium or saline treated males showed no significant differences in pre and/or post-implantation lethality at pre-meiotic, meiotic or post-meiotic stage of spermatogenesis. The groups of rats exposed to x-rays showed high incidence of post-implantation losses and a reduction in live implantations. These studies suggest that Valium lacks the potential of inducing any chromosomal damage on the germ cells of rats as revealed by the test for dominant lethal mutations.

178. Toxicological Study of Aerial Spray of Thiometon on Cattle, Goat and Poultry
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Thiometon (0,0-Dimethyl S-[2-(ethylthio) ethyl] phosphorodithioate) is an organophorous pesticide (EKATIN-Sandoz). It is designed for use in agriculture as systemic insecticide and acaricide. The formulation Ekatin-25 EC was diluted in water to 3.89% and sprayed aerially @ 9 litres (diluted mixture)/acre on the cotton field affected with the pest. The plasma cholinesterase enzyme estimation and haematological studies in cattle, goats and poultry were conducted at pre-exposure time and after exposure to aerial spray at 24 hours and 48 hours. The Posticide Thiometon (Ekatin-25 EC) did not produce toxic symptoms or any toxicity indicative of deviations in the plasma cholinesterase levels or haematological parameters in cattle, goats and poultry when exposed to the aerial spray in the concentration mentioned above.

179. Preliminary Chemical and Toxicological Investigations on Poisonous Fishes in the Coastal Areas of Bengal
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Chemical and toxicological investigations of toxins and venoms obtained from some commonly available poisonous fishes Spheroides oblongus, Dasyatis zugei) in the coastal areas of Bengal were undertaken. In the course of preliminary work in our laboratory, the toxic principles obtained by crude
extraction of liver (*Spheroides oblongus*) and sting (*Dasyatis zugei*) produced varying degrees of toxic effects including death of albino mice. The effects of these principles on the gross behaviour including affects on locomotion, sleep, food and water intake of experimental animals (monkey, rabbit, albino rat and mouse) revealed diverse results possibly related to species variations. Haematological and histological (stomach, liver and kidney) studies were also included for the determination of toxicological changes. Further isolation and purification of the toxic principles by standard physico-chemical methods are under progress.

180. **Interaction of Di-2-ethylhexyl Phthalate (DEHP) with Ethanol**

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The information on the interaction of environmental contaminants with other xenobiotics is of great significance in assessing their toxicogenic potential. Previous studies have shown that DEHP, a microchemical environmental pollutant, can prolong the pentobarbital sleeping time and modify the biological response of an organophosphorus pesticide, parathion. Effect of this widely used plasticizer was studied on ethanol sleeping time in male and female mice in the present investigation. Ethanol (3 g/kg) was injected intraperitoneally to (a) mice that had received seven successive daily doses of DEHP (3.6 ml/kg) intraperitoneally and (b) to mice 18 hrs after a single dose of DEHP. The sleeping time was recorded by 2 independent individuals not aware of the protocol. The ethanol sleeping time was reduced (25-30%) in mice following repeated doses of DEHP and was prolonged (60-80%) in animals following a single dose of the plasticizer. No significant sex difference was observed in this effect of DEHP. The results suggest that DEHP may alter the duration of action of ethanol perhaps by interfering with its metabolic disposition.

181. **Toxic Effects of Endosulfan and its Influence on Pentobarbital Induced Hypnosis in Animals**

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Endosulfan is one of the important member of the cyclodiene group and has a wide spread use for crop protection in the field of agriculture. The toxicity of this preparation was determined in various species of animals. Rats, mice and rabbits of either sex were given various doses of endosulfan in different vehicles and LD50
was determined. This study indicated sex variation in rats. In another set of experiments, rats were given repeated doses of endosulfen (0.1, 2.5 and 5.0 mg/kg) orally daily for 7 or 15 days and the effect of endosulfan on body weights, organ weights and on pentobarbital hypnosis was investigated. The tissues were examined for histopathology. There was increase in liver weight, decrease in pentobarbital ST and decreased levels in blood and brain, probably indicating hepatic-microsomal enzyme stimulation. The detailed results along with its physiological implications of this study will be discussed.

182. Preliminary Chemical and Toxicological Investigations on Poisonous Fishes in the Coastal Areas of West Bengal

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Chemical and toxicological investigations of toxins and venoms obtained from Spheroides oblongus (SO) and Dasyatis zugei (DR) off the coastal areas of West Bengal were undertaken. The oil obtained from concentrating the acetone-extract of the liver of SO gave positive Dragendorff’s test indicating the presence of alkaloid in the oil. The sting extract of DZ was protinaceous in nature. Following i. p. administration of different doses (mg/kg) of these extracts, the effects on the gross behaviour, locomotion, food and water intake of laboratory animals (monkey, 0.75 to 1.5; rabbit, 2-10; albino rat, 3-7; and mice, 0.75-3) indicated varying degrees of CNS-depression. Decrease of spontaneous motor activity, enhancement of pentobarbitone-induced sleeping time and antagonism of d-amphetamine-induced toxicity in aggregated mice (treated with sublethal doses) further suggested a possible depressant effect on the motor cortex. The different animals used in the present study, however, showed species variations as regards fatality. Although not conclusive, the histological findings of liver, kidney and gastric mucosa of rabbits killed by (10 mg/kg of SO liv. extract) suggested mild cytotoxic effects. Further chemical analysis and toxicological evaluation of the extracts are under progress.