NEW REMEDIES

The asterisk (*) after the name of an article indicates that the information given is derived from the makers' publications. Further information regarding these articles may be obtained by application to the Editor.

Anaxeryl.* The active ingredients of this ointment are dioxyanthranol 0·22 per cent., ichthyol 0·85 per cent., balsam of Peru 1·00 per cent., salicylic acid 0·30 per cent., resorcin 0·20 per cent., and birch tar oil 0·30 per cent. It is indicated in psoriasis, persistent dry eczema, lichen planus and various mycotic infections. Anaxeryl ointment may be applied daily to any part of the body. It is supplied in 40 g. tubes. A. O.

Chloroquine Diphosphate. (*New and Non-official Remedies, J. Amer. med. Ass.*, 1948, **136,** 1049.) Chloroquine diphosphate is 7-chloro-4-(4-diethylamino-1-methylbutylamino)-quinoline diphosphate, $C_{18}H_{32}O_8N_3ClP_2$; mol. wt. 515·88. It occurs as a white crystalline powder, m.pt. 193°C. to 195°C., or for a second form of chloroquine diphosphate the m.pt. is 215°C. to 218°C., readily soluble in water, almost insoluble in alcohol, benzene, chloroform and in ether; a 1 per cent. aqueous solution has *p*H about 4·5. It has a bitter taste. When dried *in vacuo* over phosphorus pentoxide at room temperature for 48 hours, it loses not more than 2 per cent. of its weight. When a few drops of ammonium molybdate solution are added to 50 mg. dissolved in 3 ml. of water, a white precipitate is produced immediately. On adding 5 ml. of a saturated aqueous solution of picric acid to 20 ml. of a 0·1 per cent. aqueous solution of chloroquine diphosphate, a yellow precipitate is immediately produced, which melts, after washing and drying, between 205°C. and 210°C. (Caution is required for this test !) When 50 ml. of a 0·5 per cent. solution, made alkaline with 1 ml. of strong ammonia solution, is extracted with two quantities, each of 30 ml. of cyclohexane, and evaporated to dryness and allowed to crystallise in a vacuum desiccator over phosphorus pentoxide, the crystals obtained have m.pt. 87°C. to 90°C. *Assay for phosphorus*—50 ml. of a 1·5 per cent. acid solution of bismuth subnitrate is added to 0·2 g., accurately weighed, dissolved in 50 ml. of water, the mixture is digested for 2 hours on a steam-bath, and filtered through a Gooch crucible; the precipitate is washed with dilute nitric acid (2 ml. in 100 ml.), water, alcohol and finally ether, and then dried for 2 hours at 100°C. and weighed. The phosphorus content is not less than 11·8 per cent. and not more than 12·25 per cent. *Assay for chloroquine diphosphate*—0·2 g. accurately weighed, is dissolved in 50 ml. of water, and the solution, made alkaline with 5 ml. of ammonia solution, is extracted with successive quantities of 25, 20, 15, 10 and 10 ml. of ether. The combined ether extracts are filtered and evaporated and the residue, after drying at 100°C. for 30 minutes, is not less than 98 per cent. and not more than the equivalent of 102 per cent. Chloroquine diphosphate is highly active against the erythrocytic forms of *Plasmodium vivax* and *P. falciparum* and is said to have about 3 times the activity of mepacrine against these organisms. It suppresses acute attacks of malaria but is not a prophylactic agent. It is administered by mouth, before or after meals; for suppression of vivax infection 0·5 g. at weekly intervals is recommended; for treatment of acute attacks of vivax or falciparum malaria an initial dose of 1 g. followed by 0·5 g. after 6 to 8 hours and 0·5 g. daily for 2 days is sufficient to terminate the attack. L. H. P.

Depropanex* is a deproteinated pancreatic extract. It is a saline solution of a chemically derived, protein-free, nitrogenous fraction obtained by acid-

alcohol treatment of mammalian pancreas. Depropanex contains no insulin, histamine or acetylcholine, and not more than 2·5 per cent. of solids of which 0·9 per cent. is sodium chloride and 0·5 per cent. is non-protein nitrogen. The *p*H is adjusted to 6·5 to 6·8. Standardisation is carried out by comparing the effect of the extract on the arterial blood pressure of anæsthetised dogs with that of a standard extract. Each batch is adjusted to contain 10 depressor units per ml. A qualitative test is made by observing the heart-blocking effect in mice. The lowering of arterial blood pressure in urethanised rabbits and atropinised dogs is used as a test for the absence of histamine and acetylcholine. Depropanex has been successfully used in intermittent claudication, especially that associated with occlusive arterial disease, in renal and ureteral colic, spastic ureteritis and dysmenorrhœa. In chronic vascular disease 2 to 3 ml. should be given intramuscularly every other day. For ureteral colic or where there is acute contraction of smooth muscles 3 to 5 ml. should be given. An intramuscular dose of 2 to 4 ml. is recommended for primary dysmenorrhœa. It is not advised that depropanex be injected intravenously. The product is supplied in 10 ml. rubber-capped vials. A. D. O.

Mycil* is a fungicide, issued in the form of an ointment and a dusting-powder, the active ingredient of which is *p*-chlorophenyl-α-glycerol ether. It is effective against *Epidermophyton floccosum* and the various species of *Tricophyton*, the usual causative organisms of athlete's foot. The ointment is used for treatment of the infection, and the dusting-powder is sprinkled in the socks or shoes as a prophylactic measure. S. L. W.

Neurinase* is a combination of the active principles of fresh valerian with soluble barbitone. It is claimed that volatile oil containing bornyl *iso*valerianate, obtained from the fresh rhizome, acts synergetically with the barbiturate. Neurinase is indicated as a hypnotic in insomnia of nervous origin and as a sedative in psycho-neurotic disorders and migraine. It is issued as a solution, containing in a teaspoonful about 2 gr. of soluble barbitone, and in tablets, containing, in each, about 3·3 gr. of soluble barbitone. S. L. W.

Nitrogen Mustard Hydrochloride,* is di-(2-chloroethyl)methylamine hydrochloride, the nitrogen mustard derivative known in America as bis(β-chloroethyl)amine hydrochloride, or "Bis." It is indicated in cases of Hodgkin's disease which have become resistant to radiation therapy, producing a remission of symptoms, and rendering the case amenable to further X-ray treatment. It does not appear to be more effective therapeutically than radiation therapy in the treatment of lymphosarcoma or lymphatic and myelogenous leukæmia. The results obtained with nitrogen mustard in the treatment of polycythæmia rubra are comparable with those obtained with radio-active phosphorus. It is administered intravenously in a dose of 0·1 mg./kg. of bodyweight for a total of 3 to 6 days; the maximum single dose should not exceed 8 mg. and an interval of 6 to 8 weeks should be allowed between courses of injections. Solutions for injection must be freshly prepared, 10 ml. of a 0·9 per cent. sterile solution of sodium chloride being added to 10 mg. of the salt. Nausea and vomiting and a tendency to hæmorrhage may occur. Extravasation should be avoided. Nitrogen mustard hydrochloride is issued in boxes of 10 vials each containing 10 mg. S. L. W.

Promizole* is a proprietary brand of 2: 4′ diamino-5-thiazolylphenyl sulphone, and is used in the oral treatment of leprosy. No claim is made as to the ultimate value in leprosy of promizole given orally, but the therapeutic results so far

obtained are considered sufficiently encouraging to warrant further clinical study. Doses of 1·5 g., increasing to 6 g., have been given daily for periods of a year or more; the drug is well tolerated. Initial clinical reports indicate that it may also be of value in tuberculosis. Tablets of 0·5 g. are supplied in bottles of 100 and 1,000. S. L. W.

Prothricin* is an antibiotic nasal decongestant which contains 2·00 per cent. of tyrothricin and 1·5 per cent. of propadrine hydrochloride. The solution is buffered to *p*H 5·5 to 6·5 and contains 0·002 per cent. of phenylmercuric acetate as a preservative. The shrinking effect of propadrine on the nasal mucosa lasts for 2 hours and causes little or no irritation or side reactions. Prolonged use does not cause the ill-effects of ephedrine on the nasal mucosa. The extensive use of tyrothricin has not given rise to drug sensitivity nor has has it caused tissue damage. In this respect it is superior to the sulphonamides. The concentration of tyrothricin in prothricin is effective in the presence of body fluids and tissue exudates against the Gram-positive organisms commonly infecting the respiratory tract and it is moderately effective against the Gram-negative meningococci and gonococci. It is recommended for acute catarrhal rhinitis, rhinosinusitis and ethmoiditis, and the incidence of otitis media and other complications may be reduced by its use. Chronic infections respond less readily. Applied by means of a dropper or spray, prothricin should be used every 15 to 30 minutes or as necessary. Unless there is constant medical supervision it is contra-indicated in heart or thyroid disease, high blood pressure and diabetes; otherwise prothricin seldom causes side effects. The preparation is supplied in dropper-bottles containing 1 fl. oz. A. D. O.

Scobenol* is a stable emulsion containing 25 per cent. of benzyl benzoate for the treatment of scabies. After bathing and drying, the emulsion is applied over the whole body from the neck downwards with a flat paint brush, and is allowed to dry on. Two such treatments, either on successive days or within a period of 8 days, are sufficient. Scobenol is issued in bottles containing 4 fl. oz., which is sufficient for the complete treatment of an adult. S. L. W.

T.E.A.B.* is a proprietary form of tetraethylammonium bromide supplied as a 10 per cent. solution for intramuscular or intravenous injection. The tetraethylammonium ion produces a fall in blood pressure, depression of gastro-intestinal motility, pupillary changes, cessation of sweating, dry mouth, and postural hypotension. It should not be administered to patients with low blood pressure or with vasomotor instability, and only with caution to patients with severe hypertension and poor renal function. It is indicated in the treatment of peripheral vascular disease and functional vascular disorders such as Raynaud's syndrome, in thrombo-angiitis obliterans and thrombophlebitis, for the relief of pain in causalgia and in neuralgia following herpes zoster, for the relief of hypertension, and for the alleviation of the pain of peptic ulcer, abdominal cramps and diarrhœa; by distension of the bladder it also relieves pain in certain types of vesical dysfunction. The recommended dosage for intravenous use is 0·2 to 0·5 g. in 10 per cent. solution; intramuscularly the dose should not exceed 20 mg./kg. of body-weight or 15 ml. of the 10 per cent. solution, but usually 5 to 10 ml. is sufficient. Intravenous injection produces an immediate response, but the effect is less prolonged than with the intramuscular injection. It is issued in boxes of 12 and 25 ampoules, each ampoule containing 1 ml. or 5 ml. of 10 per cent. solution. S. L. W.

NEW REMEDIES

Tivlolac* is a solution of colloidal calcium and vitamin D for injection, subcutaneously or intramuscularly, in allergic states such as urticaria, allergic rhinorrhœa, migraine and asthma, or in vasomotor disorders such as chilblains or angioneurotic œdema. It may also be employed prior to tonsillectomy and dental extraction to reduce capillary hæmorrhage, and it may be given to hasten bony union where this is delayed owing to known calcium deficiency. The average dose is 1 ml. daily for 2 days, followed by a similar dose at 4 to 6-day intervals. Tivlolac contains 0·05 per cent. of colloidal calcium and 5000 I.U. of vitamin D in 1 ml., and is issued in boxes of 6 and 12 ampoules of 1 ml., and in rubber-capped bottles containing 15 and 30 ml. S. L. W.

Vibelan* tablets contain aneurine hydrochloride 0·5 mg., riboflavine 0·75 mg. and nicotinamide 7·5 mg. in a yeast extract base; it is claimed that the daily administration of 4 tablets supplies the normal adult requirement of these 3 vitamins, the yeast extract providing small unstandardised amounts of other members of the vitamin B group. The use of the tablets is indicated in all vitamin B deficiency states, in seborrhœic dermatoses and some forms of acne, and in patients receiving glucose-saline infusions. Since inactivation of œstrogens by the liver is impaired by vitamin B deficiency, the use of the tablets is also suggested in the treatment of functional uterine hæmorrhage and other hyperœstrogenic states in either sex, including benign prostatic hypertrophy. Vibelan is issued in bottles of 50, 250, and 1,000 tablets. S. L. W.

THE RELATIONSHIP BETWEEN CHEMICAL STRUCTURE AND THERAPEUTIC ACTIVITY (*continued from page* 132).

With regard to the synthetic œstrogens, it was suggested that the high activity of the stilbœstrol which resulted from the work of Robinson, Dodds *et al* was due to molecular simulation of œstradiol. To probe this contention 3-monohydroxy, 4-monohydroxy and 3:4-dihydroxy-$\alpha\beta$-diethylstilbene were prepared and tested for œstrogenic activity. The 4-hydroxy compound was very active, an activity which was highly potentiated by the introduction of a second 4-hydroxy group; the 3-hydroxy derivative showed little activity, and the 3:4 dihydroxy showed a lower activity than the 4-monohydroxy compound. These results proved that molecular simulation could not be the whole story, and with any derivative of diethylstilbene a *para*-hydroxy group was of paramount importance. Further exploration of the molecular skeleton, $\alpha\beta$-diethylstilbene, has resulted in obtaining an activity similar to that of deoxycorticosterone in 4-hydroxy-4-ωhydroxyaceto-$\alpha\beta$diethylstilbene and recently cardiatonic activity in a 4-butenolide.

It will be observed that the examples chosen illustrate the empirical method of attack, but that once an activity has been obtained further work of a systematic character may be prosecuted within the group. Many thousands of different researches, having for their aim the production of something of use in medicine, have produced the comparatively few important synthetic compounds in use to-day, but, although many of the researches lead to a negative result, they none the less contribute to the knowledge of the relationship between chemical structure and therapeutic activity.