tween prostatism and atherosclerosis (Schaffner, 1972). It was also found that plasma cholesterol levels of human volunteers were decreased with daily oral administration of 300–600 mg candicidin.

Method and results: Candicidin has been orally administered to small laboratory animals for up to 15 months. Animals have been allowed normal laboratory diet and water *ad lib* and were maintained under conditions of constant temperature and humidity with a fixed light/dark schedule. Absorption of exogenous cholesterol was monitored by the use of [4–$^{14}$C] cholesterol. Candicidin and cholesterol were suspended or dissolved in arachis oil and given by stomach tube or into the mouth. Samples of whole blood, plasma, tissue or whole eviscerated animal have been treated with tissue solubiliser and radioactivity counted using a Nuclear Chicago Unilux 3 scintillation counter. All values reported here were obtained on specimens obtained 6 hours after administration of label.

Rat: Analysis of results from 13 experiments involving 120 animals in equal dosed and control groups indicates that cholesterol absorption is reduced to an average value of 23·7% control. In no experiment did absorption exceed a mean value of 39·5% (s.e.m. = 7·0) with dose of candicidin 100 mg kg$^{-1}$. The effect is similar whether the drug is given as a single dose with the cholesterol, if predosing is employed, or if the animals are dosed with candicidin and the label administered up to 24 h later.

Mouse: Acute studies indicate that absorption of cholesterol is reduced to 8·8% (s.e.m. = 0·54) of control value. Mice predosed for 15 months show cholesterol absorption at a level of 55·0% (s.e.m. = 4·70).

Other animals: Hamster, guinea-pig and rabbit show that similar effects occur in species having widely differing abilities to absorb and excrete exogenous cholesterol.

The effects reported here, of significant reductions in cholesterol absorption related to candicidin administration, are of importance in demonstrating the considerable effects of this substance on lipid metabolism in laboratory animals. Other substances including alternative polyenes and cholestyramine appear much less effective than candicidin by this screening procedure.

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**Factors in the experimental evaluation of calcium glycerophosphates in caries**

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Dietary calcium glycerophosphate (CaG) reduces the incidence of caries in experimental animals (Federoff, 1965; Bowen, 1972) and is more effective (Grenby, 1973) than the sodium salt ($\beta$-isomer). Whilst Bowen (loc. cit.) used the so-called $\beta$-isomer in monkeys, Stephen, Bealey & others (1973) using the so-called $\alpha$-isomer did not find the corresponding expected biochemical changes in plaque in children, although Brook, Gawthorpe & Winter (1973) did so to some extent. The object now is therefore to identify factors which may lead to explanation for these discrepancies.

Two types of CaG were used: '$\alpha$-isomer' (BPC 1963: predominantly $\alpha$-isomer); '$\beta$-isomer' (Sigma-actually DL-$\alpha$- and $\beta$-isomers in roughly equal proportions). Both were tableted (200 mg, plus 700 mg sucrose with or without 10 mg citric acid) under identical physical conditions. Dissolution rate in water was determined using the USP basket (100 rev min$^{-1}$) in 100 ml water; 5 ml samples were removed at 2 min intervals and the volume restored. For saliva dissolution the subject sucked a tablet, without deglutition, in the washed mouth and saliva was collected over 1 min periods. Calcium was determined flame photometrically (Williams, 1960), employing appropriate controls.

Table 1. Dissolution of CaG in water and saliva.

| Dissolution medium | Time (min) for 50% dose (Ca) to dissolve α-isomer with citric acid | α-isomer without citric acid | β-isomer with citric acid | β-isomer without citric acid |
|---|---|---|---|---|
| water | 6·6* | 14·5* | 5·8* | 17·5* |
| saliva | 2·4** | 2·9** | 2·3* | 3·1* |

Water: means of 4 tablets. Saliva: means of 4 tablets in 4 individuals. Significance of differences: $*P<0{\cdot}01$, $**0{\cdot}05>P>0{\cdot}01$.

Discrimination between CaG isomers in animal and clinical work has been referred to above although doubt exists concerning the strict identity of the isomers used. Table 1 shows that dissolution of the β-isomer in saliva is accelerated by citric acid more than that of the α-isomer although the expected general effect of citric acid is seen in water with both isomers equally. We also conclude that water and saliva are not interchangeable in dissolution studies and that dissolution rate of CaG can be modified by formulation for example by inclusion of citric acid. Future study will require much better separation and definition of isomers before definitive clinical work can be undertaken.

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**Pharmacological studies on the leaves of *Azadirachta indica***

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*Azadirachta indica* A.Juss (syn *Melia azadirachta* Linn.) is a large evergreen tree found growing in tropical and subtropical climates. It is indigenous to India and the Malay Archipelago. In addition, the tree is widely cultivated as an ornamental shade tree and has been naturalized in such countries as Nigeria, Saudi Arabia and the Soudan. In India, where it is known as the neem tree, the bark, leaves and fruit have been used from time immemorial in the treatment of such diverse complaints as constipation, fever, arthritis, worms and skin disorders.

Despite the popularity of the neem tree in folk-lore medicine, very little work has been carried out on its pharmacological properties apart from a study by Rao, Sukumar & others (1969) which indicated that neem leaves possess some antiviral activity. The present report concerns itself with other pharmacological properties possessed by neem leaves.

Young tender leaves were dried to constant weight at 40° and ground into a fine powder. A 10% w/v aqueous extract was prepared and tested for hypoglycaemic activity in rabbits (1·0–1·5 kg) previously fasted for 24 h but allowed free access to water. Following oral administration of the aqueous extract, a marked fall in blood glucose concentration was observed. This effect was both dose and time related, a maximum reduction in blood glucose level of 27% occurring 3·0 h after administration of a dose of extract equivalent to 200 mg $kg^{-1}$ dried powdered leaf. Blood glucose concentrations returned towards control levels after 12 h. A similar hypoglycaemic effect was observed in fasted rats and to a lesser extent in guinea-pigs following oral dosing.

Antidiabetic activity was dependent on the presence of functioning pancreatic beta-cells, since neem leaf extracts did not produce hypoglycaemia in totally pancreatectomized rats, or