

# A NOTE ON THE STABILITY OF THE TRIFLUOROMETHYL GROUP OF BENDROFLUMETHIAZIDE IN RATS

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The effect of bendroflumethiazide on the teeth of rats on a carious diet was examined and compared to that of sodium fluoride to determine whether release of fluoride takes place from the trifluoromethyl group of the substance. No detectable fluoride was released.

SINCE 1958 a series of fluorine-containing diuretics have appeared, the fluorine being incorporated in the molecules as a trifluoromethyl group ( $-CF_3$ ). Chemical investigations have shown that the fluorine atoms in this group are very firmly bound to the carbon atom (Kobinger, Lund and Roholt, 1960). The stability of the trifluoromethyl group in bendroflumethiazide was examined *in vivo* since release of fluoride could lead to a chronic fluorine poisoning in long term treatment with this diuretic.

Chronic fluorosis causes striking effects on the teeth which show alterations in the calcification of the enamel known as mottling, while administration of fluoride in amounts too small to produce mottling renders the teeth more resistant to caries. These observations have been used to detect the possible release of minute amounts of fluoride from the drug.

## MATERIALS AND METHODS

The method of Pindborg (1958) was used. Albino rats of the Leo Strain received *ad libitum* from the age of two months the highly cariogenic diet used by Stephan and others (1952). As an extra supplement the animals had fresh fruit and B-vitamins once weekly. They were divided into 4 groups each consisting of 10 males and 10 females.

*Group I* served as control.

*Group II* received orally by stomach tube 15 mg. bendroflumethiazide suspended in 0.2 ml. of sucrose solution per rat per day (except Sundays). This dose has a calculated fluorine content of 2 mg.

*Group III* was given 2 mg. of sodium fluoride in 0.2 ml. of sucrose solution by stomach tube per animal daily (except Sundays).

*Group IV* had 22 mg. of sodium fluoride added to each litre of drinking water, which corresponds to an average daily intake of approximately 0.9 mg. of sodium fluoride.

After 85 days of administration the rats were killed. The heads were placed in dilute NaOH solution and all soft tissue was removed. The molars were examined microscopically using bright illumination and a sharp dental explorer and the degree of caries was scored following the principles of Gustafson and others (1952). Each carious tooth was given a severity score of 1, 2 or 3 indicating a caries attack of superficial, medium or extensive type. Each rat was scored individually and the average score for each group determined.

RESULTS

In the control group, the diet produced caries in all but two animals. The number of carious teeth per rat was 2.1, the average caries severity score 2.6.

In group II, receiving bendroflumethiazide, all animals but one developed caries. The average number of carious teeth was 3.1 and the average severity score 4.1.

A marked reduction in caries was found in groups III and IV, the average number of carious teeth being 0.4 and 1.0 and the average caries severity score being 0.5 and 1.1 respectively.

Within the same group no significant difference was seen between males and females neither with regard to number of carious teeth nor to caries severity score.

It was noted that 93 per cent of the carious teeth were found among the molars of the mandible.

In group III the enamel of all incisors had a banded appearance, each white band corresponding to each dose of sodium fluoride. In marked cases we were able to locate the region of growth on Sundays (no administration) by means of the broader normal orange pigmented bands. No such rings were seen in group II.

CONCLUSION

The results clearly demonstrate the caries inhibiting effect of fluoride on rat molars (Groups III and IV). Since no inhibition was observed in rats treated with bendroflumethiazide (group II) it can be concluded that no fluoride detectable by this method was released from the trifluoromethyl group of the drug.

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