Salivary Levels of Antibiotics from Use of Neomycin-Gramicidin Chewing Troches

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Previous studies demonstrated that a neomycin-gramicidin chewing troche is effective in reducing the oral bacterial flora. The present study shows that this test preparation is highly efficient in terms of the biologic availability of the preparation's antibiotic components.

POST-TONSILLECTOMY hemorrhage due to secondary bacterial infection remains a serious complication. Systemic penicillin prophylaxis does not seem to be effective in improving the appearance of the surgical wound or in hastening healing (1). Several reported studies with a topical antibacterial chewing troche[1] indicate that this preparation has been used successfully in an attempt to control late post-tonsillectomy hemorrhage by preventing secondary local infection (1–6). However, in none of the latter studies was proof of actual reduction in the bacterial count of the oral cavity specifically sought.

More recently, an investigation (7) was undertaken in normal subjects to determine the effectiveness of this antibiotic chewing troche in reducing the oral bacterial flora. The results showed that the use of the chewing troche reduced by 50% the average bacterial count of the oral cavity. The medicated gum had a prolonged effect as evidenced by significant reduction in the oral bacterial counts three hours after chewing.

The present study was conducted in order to determine if chewing gum troches containing neomycin and gramicidin are in actuality an efficient dosage form for releasing into the saliva, over a relatively sustained period of time, significant levels of the antibiotics.

EXPERIMENTAL

Materials and Method—To determine the biologic availability of the neomycin and gramicidin components of the preparation, saliva samples were collected from five subjects over 3 consecutive 5-min. periods, during which each subject chewed one of the antibiotic gum troches. The gum cud was then removed from the mouth, and an unstimulated saliva sample was collected for a fourth 5-min. period. Antibiotic assays were then performed on each of the four saliva samples and on the gum cud. Neomycin and gramicidin assays were conducted according to the methods described by the Food and Drug Administration (8).

Procedure Used for Collecting Saliva—Five graduated 100-ml. beakers, marked S1, S2, S3, cud, and S4, were set before each subject. At the start of the test, each subject placed an antibiotic gum troche in his mouth, which he then chewed for 15 min. The subjects were asked not to swallow any saliva during the course of the test. Saliva was collected during the first 5-min. period in beaker S1. At the end of the 5-min. period, beaker S1 was removed and the second 5-min. salivary sample was collected in beaker S2. This procedure was repeated for the third 5-min. period. Then the chewing gum cud was removed and placed in the appropriately marked beaker. The subject finally collected his unstimulated saliva for an additional 5 min. in beaker S4. (All subjects later repeated the procedure when fresh salivary samples were required for repeat tests.)

Preparation of Saliva and Gum for Neomycin Assay—Preliminary tests using collected saliva indicated that saliva sample No. 1 contained about 3,000 mcg. of neomycin, saliva sample No. 2 about 200 mcg. of neomycin, saliva samples No. 3 and No. 4 less than 10 mcg., and the cud less than 1 mcg. The cud was prepared for assay by first chilling, then breaking into small pieces, then steaming for 5 hr. in 25 ml. of buffer. The suspension was then blended for 2 min. in a blender, filtered, and the filtrate used in the assay.

Preparation of Saliva and Chewing Gum Cud for Gramicidin Assay—Preliminary tests indicated that saliva sample No. 1 contained abut 150 mcg. of gramicidin, saliva sample No. 2 about 4 mcg., and saliva samples No. 3 and No. 4 and the cud approximately 0.8 mcg. The cud was prepared for assay by first freezing under dry ice. The frozen cud was then ground up and suspended in 20 ml. of alcohol. The suspension was steamed for 2 hr., blended for 2 min. in a blender, and filtered. The filtrate was then assayed.

RESULTS

The results of the neomycin assays of the salivary samples and the gum cuds are given in Table I. The mean volumes of saliva collected are also recorded in this table. An average total of 2.6 mg. of neomycin was recovered for the five subjects from the saliva and cud samples. This amounted to 74% of the claimed neomycin content (3.5 mg.). It is assumed that the unrecovered fraction of the neomycin was adsorbed on the mucosal surface of the oral cavity or was lost by swallowing.

As is apparent from the data in Table I, the greatest amount of neomycin was liberated from the chewing gum vehicle during the first 5 min. of chewing.

The results of the gramicidin assays are given in Table II. Volumes of saliva collected are also shown in the same table.

An average total of 171 mcg. of gramicidin was

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[1] Orabiotic chewing troches. Each gum troche contains: neomycin (from the sulfate), 3.5 mg.; gramicidin, 0.25 mg.; and propesin (propyl-*p*-aminobenzoate), 2.0 mg.

TABLE I—AMOUNTS OF NEOMYCIN RECOVERED

Saliva Sample 5-Min. Periods	Mcg. of Neomycin — Subjects RB	CH	BB	VW	AR	Av.
1st	1698	3226	2872	1348	2740	2376.8
2nd[a]	99	298	282	171	218	213.6
3rd[a]	3	7	7	3	3	4.6
4th[a]	3	3	3	3	3	3.0
Total	1803	3534	3164	1525	2964	2598.0
Chewing Gum Cud[a]	0.8	0.5	0.8	0.5	1.0	0.7
Total	1803.8	3534.5	3164.8	1525.5	2965.0	2598.7
Saliva	Volume of Saliva Collected, ml.					
1	12	15	12	10	18	13.4
2	10	12	10	8	15	11.0
3	10	8	10	8	10	9.2
4	5	5	5	5	8	5.6

[a] Approximate values.

TABLE II—AMOUNTS OF GRAMICIDIN RECOVERED

Saliva Sample 5-Min. Periods	Mcg. of Gramicidin — Subjects RB	CH	BB	VW	AR	Av.
1st	146.0	183.0	189.0	130.5	180.0	165.7
2nd	3.3	2.8	2.0	1.6	5.4	3.0
3rd	0.2	1.3	0.2	0.8	0.1	0.5
4th	0.3	0.6	0.2	0.2	0.1	0.3
Total	149.8	187.7	191.4	133.1	185.6	169.5
Chewing Gum Cud[a]	1.5	1.6	1.5	1.7	1.7	1.6
Total	151.3	189.3	192.9	134.8	187.3	171.3
Saliva	Volume of Saliva Collected, ml.					
1	20	15	15	15	20	17
2	15	12	10	10	18	13
3	10	8	8	8	18	10
4	6	6	8	8	10	7

[a] Approximate values.

recovered from the saliva and cud samples. This amounted to 68% of the claimed gramicidin content of the chewing troche (0.25 mg.). It is assumed, as with the neomycin, that the unrecovered fraction of the gramicidin was adsorbed on the tissues of the oral cavity or was lost by swallowing. As shown by the data summarized in Table II, the greatest amount of gramicidin was liberated from the troche during the first 5 min. of chewing.

SUMMARY AND CONCLUSION

The data indicate that the chewing gum vehicle of the test preparation is highly efficient in terms of the biologic availability of the preparation's antibiotic components. The average amounts of neomycin and gramicidin retained in the gum vehicle after 15 min. of chewing were negligible.

Most of each antibiotic component was liberated during the first 5 min. of chewing. The average amount of neomycin liberated after 15 min. of chewing approximated 74% of the labeled neomycin content of the troche. The average amount of gramicidin assayed from the saliva during the same period was approximately 68% of the labeled gramicidin content of the troche.

The unrecovered fractions of the neomycin and gramicidin were undoubtedly swallowed or adsorbed on the oropharyngeal mucosa. Further, the assay data indicate that, particularly during the first 10 min. of chewing, salivary levels of neomycin and gramicidin were maintained, which far surpassed the inhibitory levels required to suppress the growth of the oral flora.

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Keyphrases

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