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DESIGN AND EVALUATION OF TINIDAZOLE DENTAL IMPLANTS

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ABSTRACT

Tinidazole dental implant was formulated, in vitro release, stability and in vivo therapeutic efficacy of these dental implants were evaluated. Tinidazole dental implant had efficient antibacterial activity with 400 times decreased dose.

INTRODUCTION

Dental diseases are recognized as a major public health problem throughout the world. Since dental diseases may be chronic, long-term treatment is often necessary.[1] The effective use of antibacterial agents for the treatment of periodontal diseases requires an adequate drug concentration at the site of action and a means to maintain that level for a sufficient duration. The periodontal pocket is an important site for this form of therapy, since it is the source of continued

localized infection.[2] Targeting a particular drug to a desired site, minimizes superfluous distribution of the drug to other body organs. In our studies, sustained release of drug was achieved by embedding tinidazole in different polymers.

MATERIALS AND METHODS

Preparation : Ethyl cellulose with or without copolymer was dissolved slowly by adding dry powder to ethanol which was vigorously stirred. Tinidazole powder was mixed after complete dissolution of the polymer. Films of suitable thickness were cast from ethanol solution after transferring into petridish. The films were allowed to dry completely.[3] The sheets of film were cut into rectangles of varying dimensions ranging from 5 mm in width and 5 mm in length. The thickness of the films was in the range of 160 to 180 mcm. These rectangles served as the sustained release devices (S.R.D.) (Table No. 1).

Stability Kinetics : Various types of dental implants were subjected for accelerated stability studies at 37°C, 45°C and 80% RH.

In Vitro Release : Different sets of dental implants, containing tinidazole (3.6 mg) were placed in 5 ml vials containing 1 ml of distilled water at 37°C for 24 hours. The amount of tinidazole released was analysed spectrophotometrically at 368 nm. Cumulative release of tinidazole from various dental implants were determined for 14 days[4] (Table No.2).

Table No. 1

IN VITRO RELEASE AND STABILITY OF TINIDAZOLE DENTAL IMPLANTS

Tinidazole Dental Implant	K at 25°C ($Days^{-1}$)	$t_{10\%}$ Values at 25°C (days)	Cumulative Release of Tinidazole after 14 days(mcg)
a) Ethyl cellulose [E.C]	2.096×10^{-3}	35.78	1192.17
b) E.C + Eudragit [Rs 100]	5.102×10^{-3}	50.38	1160.92
c) E.C + Eudragit [L 100]	3.946×10^{-3}	26.35	1007.40
d) E.C + HPMC [50 CPS]	1.960×10^{-3}	53.06	941.28
e) E.C + PEG 6,000	5.070×10^{-3}	20.51	701.15

$t_{10\%}$ values at high humidity for preparation (d) - 49.57 days.

Table No. 2

IN VITRO RELEASE OF TINIDAZOLE FROM DENTAL IMPLANTS PREPARED WITH THE COMBINATION OF ETHYL CELLULOSE AND HPMC (50 cps) HAVING 5/5 DIMENSION)

Days	Average Release of Tinidazole from 5 Implants (mcg)	± S.D.	Cumulative Amount of Drug Released (mcg)
1.	523.36	14.90	525.36
2.	297.40	75.50	822.76
3.	46.80	15.10	869.56
4.	32.00	21.74	901.56
5.	11.40	7.86	912.96
6.	6.08	3.68	919.04
7.	4.96	3.67	924.00
8.	5.60	1.15	929.60
9.	2.92	1.17	932.52
10.	2.68	0.57	935.20
11.	3.40	0.824	938.60
12.	1.96	0.909	940.56
13.	0.72	1.18	941.28

Table No. 3

CLINICAL EVALUATION OF TINIDAZOLE DENTAL IMPLANTS PREPARED WITH THE COMBINATION OF ETHYL CELLULOSE AND HPMC (50 cps)

Blank : 100% Transmittance

S.No.	Patient Code	Percentage of Transmittance					
		0 Without Scaling	7th Scaling	14th	0 With Scaling	7th	14th
1.	P	18.0	80.2	87.4	27.0	93.4	94.1
2.	Q	57.8	87.9	91.2	69.4	88.8	92.2
3.	R	58.9	89.6	93.0	45.4	94.4	98.2
4.	S	61.0	87.0	91.2	58.0	82.2	90.6
5.	T	49.8	79.2	81.4	54.0	71.0	79.2
6.	U	18.0	82.8	89.0	21.0	86.0	88.9
Control	V	23.2%	19.4%	18.0%	31.0%	22.0%	19.1%

In Vivo Studies : Controlled release tinidazole dental implants were placed in 6 patients. Bacterial samples (plaque) were collected from the periodontal pockets using upward strokes with the help of gracy curette. The material thus retrieved was dispersed in 5 ml of sterile solution of 1% gelatin in sterile saline.[5] From this solution with the help of a micro pipette a measured quantity (50 ul) of the solution was taken and innoculated in 10 ml of sterile thioglycollate medium

and incubated at 37°C for overnight and the transmittance was measured at 530 nm using Spectronic 20D (Table No. 3). Increase in the transmittance of the light was related to the inhibition of the microorganisms.

RESULTS AND DISCUSSION

In Vitro Release : The release pattern of tinidazole (for 14 days) from the implant prepared with combination of Ethyl cellulose (80%) and HPMC (20%) was found to be the best. The extent of release of tinidazole from this dental implant was maintained for more number of days.

Stability Studies : From the stability studies of tinidazole in different dental implants conducted at R.T. 37°C, 45°C and at 80% RH, it was observed that tinidazole in dental implant prepared with the combination of ethyl cellulose and HPMC was more stable than in the implant prepared with the combination of other polymers (Table No. 1).

Clinical Evaluation : Tinidazole dental implants prepared with the combination of ethyl cellulose and HPMC polymers were selected for the clinical studies, because of better in vitro release pattern (Table No.2), and lower degradation rate constant. The system described here provides the controlled release of an antibacterial agent over a period of 7 days. The selection of the S.R.D. was based on the assumption that 7 days of Tinidazole exposure at an effective dose was adequate for initial clinical trials. It gives adequate release of tinidazole and after 7 days it can be replaced by a new S.R.D. if necessary.

In periodontitis the depth of pockets in this part of the study was in the range between 6-9 mm, and the dimensions of the initial strip placed for first 7 days was 5 mm in length and 3 mm in width. There was a positive result in treatment and the depth of the pocket was decreasing (measured with help of probe). For the second week study the strip dimensions were changed to 3 mm in length and 3 mm in width. The percentage transmittance of the light through bacterial medium was related to extent of the growth and inhibition of the bacteria after the incubation at 37°C for overnight.

The results of the treatment by tinidazole dental implants were compared with the effect of tinidazole dental implants with scaling. But, it was observed that the result was found to be similar in case of these two conditions. The extent of the inhibition of the bacteria was observed as high in case of the first week study and the treatment was followed to get further result. At the end of second week, the extent of inhibition of the microorganism seems to be almost similar to normal healthy volunteer's plaque. In case of control the bacterial growth was found to be increasing gradually along with the time period (Table No. 3).

CONCLUSION

This study showed that the release of tinidazole from dental implant prepared with combination of Ethyl cellulose and HPMC was in a sustained pattern. By the stability studies among all the tinidazole dental implants, the one which was prepared with the combination of Ethyl cellulose and HPMC (50 cps) was

found to be most stable and the one which was prepared with the combination of Ethyl cellulose and PEG (6000) was found to be having higher degradation rate.

The results obtained from the clinical studies of tinidazole dental implant indicated that the S.R.D. effectively alters the bacterial population of the periodontal pockets by reducing the bacterial growth and it has been proved that the placing of dental implant after scaling was not more effective. The major advantage of the local application of antibacterial agents in an S.R.D. form are limiting the drug to it's target site, the local concentration achieved can be much higher than is possible via the systemic route and reduction of the total patient dose by over 400-fold. This method of treatment will be promising alternative for the treatment of periodontitis.

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