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FORMULATION DEVELOPMENT AND *IN VITRO* EVALUATION OF BUCCAL TABLETS OF TERBUTALINE SULFATE

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Abstract:

The buccal terbutaline sulfate tablets were developed utilizing a direct compression method and several grades of HPMC polymers, such as K4M, K15M, and K100 M, with varied ratios and effects on drug release. The produced buccal tablets were tested in pre and post-compression studies. All formulation findings have been determined to be within pharmacopeia limitations. The most significant percentage of drug release for 10 hrs was 99.14% in the optimized formulation (F2) with HPMC K4M (15%), and the strength of the bioadhesive was determined to be 31.64 gm. F2 formulation, drug release kinetics followed zero-order release kinetics.

Keywords: *Terbutaline sulfate, buccal tablets, HPMC, and bioadhesive strength*

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1. INTRODUCTION:

Buccal administration is an enteral mode of administration that allows medications to pass past the mouth mucosa and into circulation. Because the drug does not transit through the digestive system and avoids first-pass metabolism, buccal administration may give higher bioavailability and a faster onset of action than oral administration [(1)]. Terbutaline sulfate (TS) is a bronchodilator and tocolytic that is a selective beta-2 adrenergic agonist. It helps patients with asthma, bronchitis, emphysema, and other lung illnesses avoid bronchospasm [(2)]. The current study seeks to develop the buccal administration of TS utilizing different grades of HPMC polymers.

2. MATERIALS AND METHODS:

2.1. Materials

Terbutaline sulfate was provided as a gift sample from Natco Pharma, Hyderabad. HPMC grades and lactose were supplied from Merck Specialities Pvt Ltd, Mumbai, India. Talc and Magnesium stearate was from Neutron Drugs and Pharmaceuticals Pvt Ltd, Hyderabad. All other chemicals and reagents are analytical grade were used in the study.

2.2. Methods

2.2.1. Formulation development of Buccal Tablets

Direct compression was used for developing the formulations. All additional components, including TS (API), were separately sieved via sieve no 40. They were triturated for up to 10 minutes and adequately combined with all ingredients. Talc was used to lubricate the powder mixture. (3). The tablets were made in the manner described below. The total weight of the tablet was 100mg. Table 1 shows the components of several formulations.

Table 1: Composition of buccal tablets formulation

Formulation code	TS	HPMCK 4M	HPMCK 15M	HPMCK 100M	Magnesium Stearate	Talc	Lactose
F1	5	10	-	-	5	5	75
F2	5	15	-	-	5	5	70
F3	5	20	-	-	5	5	65
F4	5	-	10	-	5	5	75
F5	5	-	15	-	5	5	70
F6	5	-	20	-	5	5	65
F7	5	-	-	10	5	5	75
F8	5	-	-	15	5	5	70
F9	5	-	-	20	5	5	65
The total weight of each tablet is 100mg							

2.2.2. Evaluation of post-compression parameters

The designed formulation tablets were studied for their weight variation, hardness, friability, and drug content.

Weight variation test:

Twenty tablets were taken to study the weight variation, and their weight was determined individually and collectively on a digital weighing balance. The average weight of one tablet was determined from the collective weight [(4)]. The percent deviation was calculated using the following formula.

% Deviation = (Individual weight – Average weight / Average weight) × 100

Hardness test

Tablet hardness was measured using a Monsanto hardness tester. The crushing strength of the 10 tablets with known weight and thickness each was recorded in kg/cm 2, and the average hardness and the standard deviation was reported [(5)].

Friability test

The six (6) tablets were selected from each batch and weighed. Each group of tablets was rotated at 25rpm for 4min (100 rotations) in the Roche friabilator [(6)].

Drug content:

Ten tablets were finely powdered quantities of the powder equivalent to one tablet weight of TS that were accurately weighed, transferred to a 100 ml volumetric flask containing 50 ml water, and allowed to stand to ensure complete solubility of the drug. The mixture was made up to volume with water. The solution was suitably diluted, and the absorption was determined by UV – a visible spectrophotometer [(7)].

***In vitro* drug release studies**

Drug release studies were conducted using a USP type II dissolution test apparatus and the rotating paddle method. The study was conducted at 37±0.5ºC and 50 rpm using 900 ml of 6.8 pH buffer for 12 hrs.

At regular pre-determined time intervals, aliquots of the sample (5 ml) were taken out, diluted appropriately, and the drug concentration was evaluated using a UV spectrophotometer at 270 nm [8].

***In-vitro* bio-adhesion studies**

Hydration of the bioadhesive polymer is required to initiate the bioadhesive bonding process (14). The formulations F1 to F3 prepared with HPMC K4M had the highest adhesion force, i.e., the strongest bioadhesive bond, and the bioadhesive strength of buccal tablets was found to be 29.27 to 33.19 gms. The bioadhesive strength of formulations F4 to F6 containing solely HPMC K 15M was determined to be 27.72 to 29.56. Formulations F8 to F9 include HPMC K100M and have bioadhesive strengths ranging from 26.15 to 29.59 gm [9].

2.2.3. Drug – Excipient compatibility studies

Fourier Transform Infrared (FTIR) studies

The physical properties of the material mixture were compared with those of a plain drug. Samples were mixed thoroughly with 100mg potassium bromide IR powder and compacted under a vacuum at a pressure of about 12 psi for 3 minutes. The resultant disc was mounted in a suitable holder in a Perkin Elmer IR spectrophotometer, and the IR spectrum was recorded from 3500 cm to 500 cm. The consequent spectrum was compared for any spectrum changes [10].

3. RESULTS AND DISCUSSION:

3.1. Evaluation of pre-compression studies

The present study aimed to develop buccal tablets of TS using HPMC polymers. All the formulations were evaluated for bulk density, tapped density, compressibility index, Hausner ratio, and angle of repose were determined for the prepared powder blend [11]. All the formulations were within the range, showing the powder has good flow properties. The results are shown in Table 2.

Table 2: Pre-compression studies of powder blend

Formulation code	Angle of Repose	Bulk density	Tapped density	Carr's index (%)	Hausner's Ratio
F1	24.17 ± 0.7	0.49 ± 0.03	0.54 ± 0.04	15.82 ± 0.14	0.81 ± 0.04
F2	23.04 ± 1.4	0.62 ± 0.07	0.52 ± 0.04	16.29 ± 0.15	0.94 ± 0.06
F3	26.24 ± 1.8	0.56 ± 0.04	0.58 ± 0.05	17.35 ± 0.11	0.74 ± 0.03
F4	25.41 ± 2.1	0.54 ± 0.09	0.54 ± 0.07	16.82 ± 0.18	1.28 ± 0.07
F5	24.39 ± 1.9	0.59 ± 0.02	0.57 ± 0.03	15.91 ± 0.14	1.32 ± 0.08
F6	24.25 ± 0.8	0.55 ± 0.06	0.56 ± 0.06	17.56 ± 0.19	1.16 ± 0.09
F7	25.72 ± 1.5	0.52 ± 0.08	0.59 ± 0.04	16.32 ± 0.13	0.81 ± 0.03
F8	24.04 ± 1.8	0.57 ± 0.04	0.67 ± 0.02	17.07 ± 0.17	1.19 ± 0.09
F9	25.28 ± 2.3	0.54 ± 0.05	0.5 2 ± 0.03	17.19 ± 0.15	1.27 ± 0.02

3.2. Evaluation of post-compression studies

The developed buccal tablets of TS were evaluated for post-compression studies such as hardness, friability, thickness, weight variation, and assay for all the formulations [12]. The results were found to be within acceptable limits. The results are presented in Table 3.

Table 3: Post-compression parameters of buccal tablets

Formulation codes	Weight variation (mg)	Hardness (kg/cm2)	Friability (%)	Thickness (mm)	Assay (%)
F1	98.57 ± 2.87	5.7 ± 0.18	0.45 ± 0.05	2.9 ± 0.03	98.75 ± 1.92
F2	101.42 ± 1.76	5.6 ± 0.16	0.58 ± 0.03	2.4 ± 0.02	99.14 ± 2.23
F3	98.67 ± 2.56	5.4 ± 0.12	0.53 ± 0.09	2.7 ± 0.01	99.42 ± 2.85
F4	101.57 ± 3.75	5.8 ± 0.14	0.49 ± 0.06	2.8 ± 0.02	98.69 ± 2.13
F5	99.48 ± 1.89	5.7 ± 0.15	0.60 ± 0.04	3.0 ± 0.01	99.42 ± 2.31
F6	100.71 ± 2.95	5.5 ± 0.17	0.63 ± 0.02	2.6 ± 0.03	98.38 ± 3.41
F7	102.30 ± 2.31	5.4 ± 0.14	0.54 ± 0.03	2.8 ± 0.02	98.85 ± 2.92
F8	101.25 ± 1.91	5.9 ± 0.11	0.59 ± 0.02	2.2 ± 0.01	99.62 ± 2.57
F9	98.34 ± 2.86	5.6 ± 0.19	0.67 ± 0.07	2.5 ± 0.02	99.13 ± 2.19

3.2.1. *In vitro* release studies

The formulations (F7-F9) were prepared with HPMC K100M as the polymer was unable to retard the drug release up to desired period, i.e., 10 hrs. The formulations (F4-F6) prepared with HPMCK15M showed more retardation after 10 hrs; they did not demonstrate total drug release. Hence they were not considered. Whereas the formulations (F1-F3) were prepared with HPMC K4M retarded the drug release in the concentration of 15mg (F2) showed the required release pattern, i.e., retarded the drug release up to 10 hrs and showed a maximum of 99.14% in 10 hrs with good retardation [13]. The results are shown in Figure 1.

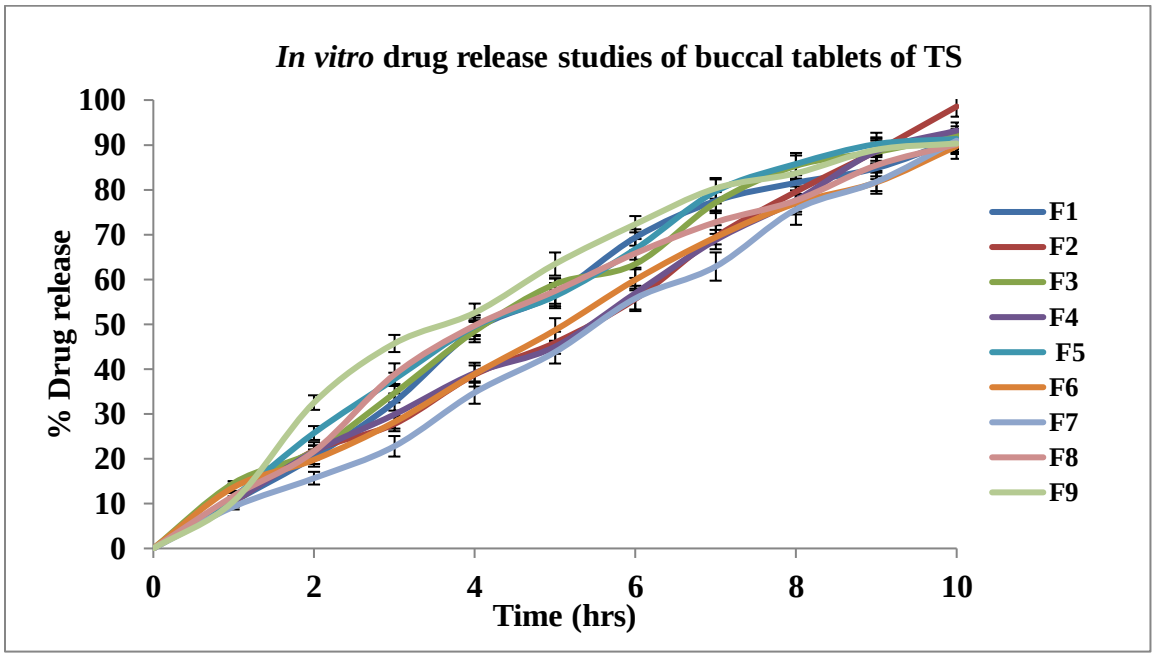

Figure 1: Dissolution profile of buccal tablets of TS

3.2.2. *In-vitro* bio-adhesion studies:

Hydration of the bioadhesive polymer is essential to initiate bioadhesive bonding [14]. The highest adhesion force, i.e., the highest strength of bioadhesive bond, was observed with formulations F1 to F3 prepared by using HPMC K4M, and the bioadhesive strength of buccal tablets was found to be 29.27 to 33.19 gms. The formulations F4 to F6 contained only HPMC K 15M, and bioadhesive strength was 27.72 to 29.56. Formulations F8 to F9 have HPMC K100M and show bioadhesive strength of 26.15 to 29.59 gm, respectively.

3.3. Release kinetics

The optimized formulation was subjected to drug release rate kinetics; the obtained data were fitted into zero-order, first-order, Higuchi, and Korsmeyer-Peppas release models [15]. The graphs concluded that formulation F2 followed Zero order release kinetics. The results are shown in Figure 2.

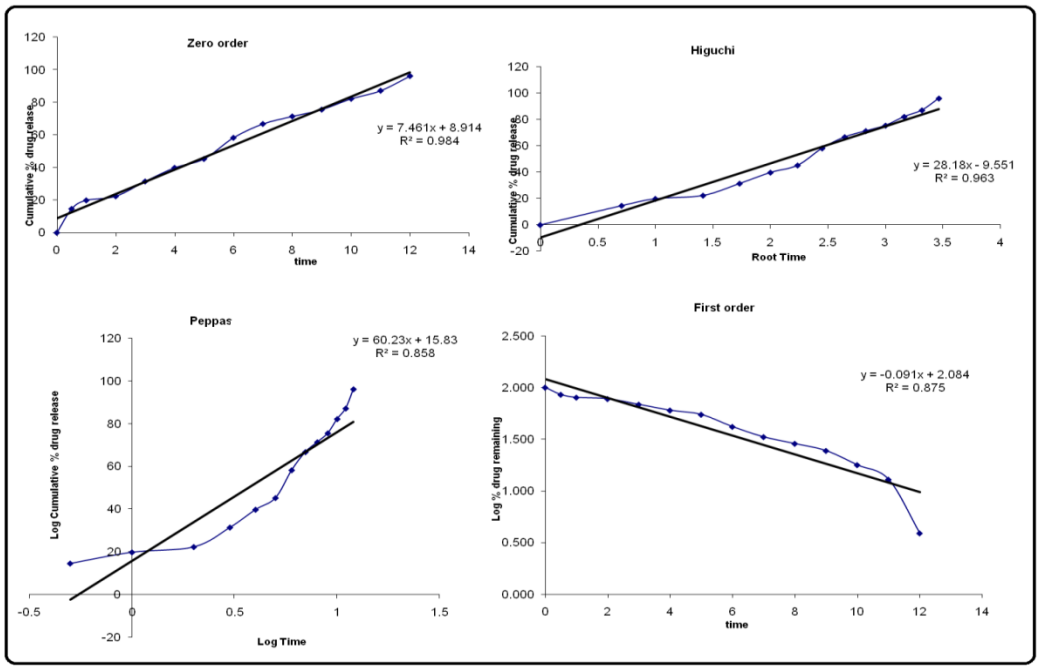

Figure 2: Release kinetics of buccal tablets of TS

3.2.4. Drug and Excipient compatibility studies

The FTIR spectra of TS and its optimized formulation with HPMC K4M polymer are shown in Figure 3, in these studies indicated no interaction between TS and polymers.

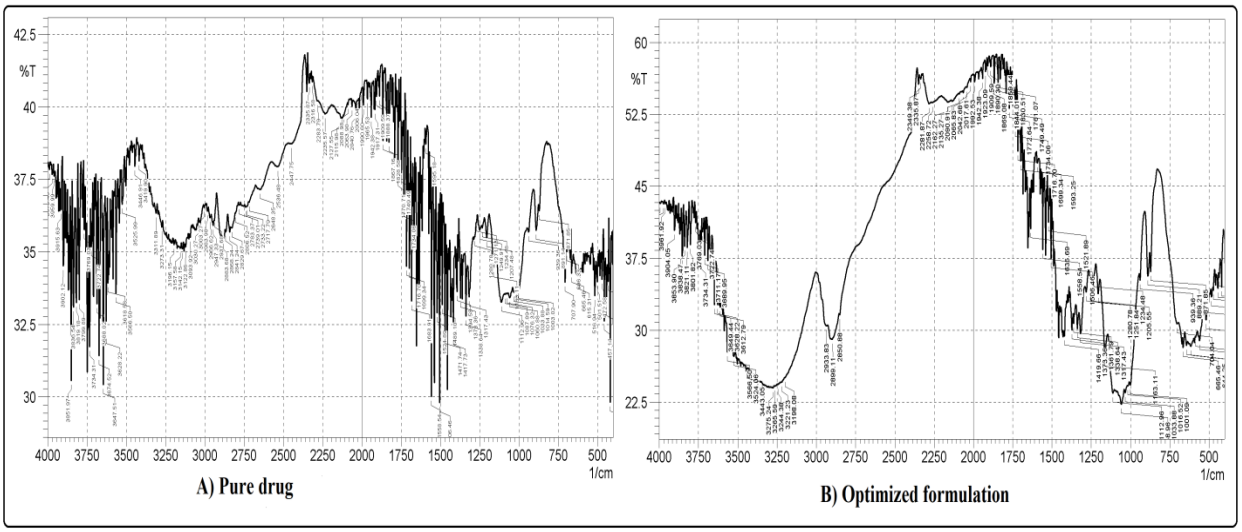

Figure 3: FTIR spectrum of pure drug & optimized formulation

4. CONCLUSION:

The present work to develop buccal tablets of TS was prepared by direct compression method. Different polymers in different ratios were tried to select the optimum formulation. They were selected based on their effect on the retardation of drug release from a tablet. The physicochemical parameters tested for the formulations, released studies, and mathematical models showed promising results. It is concluded that novel formulations can release drugs for an extended period. Whereas from the dissolution studies, it was evident that the formulation (F2) showed better and

retarded drug release 99.14% in 10 hrs, the formulation prepared by HPMC K4M was offered the highest strength of bioadhesive bond, and it followed zero order release kinetics.

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