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Novel Approach in Designing and *In-Vitro* evaluation of Mouth Dissolving Tablets of Metoclopramide Hydrochloride

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ABSTRACT

The purpose of the present work was to design Mouth dissolving tablets of Metoclopramide Hydrochloride by incorporating clove oil, which acts as flavoring and local anesthetic agent on the surface of the taste buds. Additionally Stevia leaf Powder was incorporated as sweetening agent which is 400 times sweeter than Sucrose. The tablets were prepared by direct compression technique. The formulated tablets were evaluated for Pre formulation and post formulation parameters and they were found to be satisfactory. Direct compression method was employed for making mouth dissolving tablets. The formulated mouth dissolving tablets possessed good drug releasing property, good mouth feel and improved drug availability with better patient compliance.

Keywords: Mouth dissolving tablet, Metoclopramide Hydrochloride, clove oil.

INTRODUCTION

Patients, particularly pediatric and geriatric patients, have difficulty in swallowing solid dosage forms. These patients are unwilling to take these solid preparations due to a fear of choking. In order to assist these patients, several mouth dissolving drug delivery systems has been developed. Mouth dissolving tablets can be prepared by direct compression, wet granulation, moulding, spray drying, freeze drying or sublimation methods [1]. Mouth dissolving tablets dissolve rapidly in the saliva without the need for water, releasing the drug [2, 3].

Metoclopramide hydrochloride a derivative of p-amino benzoic acid, which is a commonly prescribed drug used for the management of gastrointestinal disorders such as gastric stasis, gastro esophageal reflux and for the prevention of cancer chemotherapy- induced emesis [4-7].

In general, emesis is preceded with nausea and in such condition it is difficult to administer drug with a glass of water; hence it is beneficial to administer such drugs as mouth dissolving tablets. Metoclopramide HCl is an intensely bitter drug; hence, if it is incorporated directly into mouth dissolving tablets the main objective behind formulation of such a dosage form will definitely get futile.

In this study clove oil was incorporated as flavoring agent, which has additional advantage of having local anesthetic property on the surface of the taste buds [8]. The Stevia leaf (*Stevia rebaudiana*) powder was incorporated as sweetening agent which is 400 times sweeter than Sucrose [9].

MATERIALS AND METHODS

Materials

Metoclopramide Hydrochloride was a gift sample from Alembic Research Ltd, Vadodara, India. Stevia leaf powder was obtained from the medicinal garden of Sri Krishnadevaraya University, Anantapur, India and authenticated by the Botany department of Sri Krishnadevaraya University, Anantapur, India. Mannitol, Clove oil, talc, micro crystalline cellulose, Cross carmellose sodium, Cross Povidone, magnesium stearate and talc were purchased from S.D. Fine Chemicals, Mumbai, India. All other chemicals, solvents and reagents were used of either pharmacopoeial or analytical grade.

Methods

Preparation of Mouth Dispersible Tablets

All the ingredients were passed through sieve No. 60. Metoclopramide Hydrochloride, Mannitol, Micro Crystalline Cellulose and stevia leaf powder were triturated in a glass mortar. Superdisintegrants were incorporated in the powder mixture and finally magnesium stearate and talc were added as lubricant. The powder mix was weighed individually and compressed with 10mm flat face surface punches using hydraulic press single tablet punching machine [10].

Evaluation of the prepared tablet: [11-14]

1) Pre-compression parameters

a) Compatibilities study

The compatibility of drug and polymers under experimental condition was conducted using FTIR studies. In the present study, the potassium bromide disc (pellet) method was employed.

b) Flow properties

The powdered blend was evaluated for flow properties viz., Angle of repose, loose bulk density (LBD), tapped bulk density (TBD), Carr's compressibility index, and hausner's ratio

2. Post compression parameters:

a) Thickness

The thickness was determined using screw gauge (Mitutoyo, New Delhi, India). 5 tablets from each batch were used and the average values were calculated.

b) Hardness test

Hardness indicates the ability of a tablet to withstand mechanical shocks while handling. The hardness of the tablets was determined using Monsanto hardness tester. It is expressed in

kg/cm^2. Three tablets were randomly picked and analyzed for hardness. The mean and standard deviation values were also calculated.

c) Friability test

The friability of tablets was determined using Roche Friabilator. The friabilator was operated at 25 rpm for 4 minutes or run up to 100 revolutions. The % friability was then calculated by eq.1.

$$F= W_{initial} – W_{final} / W_{initial} X\ 100 \ldots\ldots\ldots\ldots\ldots (1)$$

Where

F= Friability (%), $W_{initial}$ = initial weight, W_{final} = Final weight

d) Weight variation test

To study weight variation, 20 tablets of each formulation were weighed using an electronic balance (Denver APX-100, Arvada, Colorado) and the test was performed according to the official method.

e) Drug content uniformity

Tablet containing 8mg of drug is dissolved in 100ml of 0.1N HCl taken in volumetric flask. The drug is allowed to dissolve in the solvent. The solution was filtered, 1ml of filtrate was taken in 50ml of volumetric flask and diluted up to mark with 0.1N HCl and analyzed spectrophotometrically at 273 nm. The concentration of Metoclopramide Hydrochloride in mg/ml was obtained by using standard calibration curve of the drug. Claimed drug content was 10mg per tablet. Drug content studies were carried out in triplicate for each formulation batch.

f) Wetting time

The tablet was placed in a petridish of 6.5 cm in diameter, containing 10 ml of water at room temperature, and the time for complete wetting was recorded. To check for reproducibility, the measurements were carried out six times and the mean value calculated.

g) Water absorption ratio

A piece of tissue paper folded twice was placed in a small petridish containing 6ml of distilled water. A tablet was put on the paper and time required for complete wetting was measured. The wetted tablet was then weighed. Water absorption ratio, R, was determined using eq.2

$$R = 10\ X\ \frac{(Wa – Wb)}{Wb} \qquad \ldots\ldots. (2)$$

Where,

Wb = weight of the tablet before water absorption

Wa = weight of the tablet after water absorption

Three tablets from each formulation were analysed performed and standard deviation was also determined.

h) In vitro dispersion time

Tablet was placed in 10 ml phosphate buffer solution, pH 6.8±0.5^{o}C. Time required for complete dispersion of a tablet was measured.

i) In-vitro disintegration time

The process of breakdown of a tablet into smaller particles is called as disintegration. The *in-vitro* disintegration time of a tablet was determined using disintegration test apparatus as per I.P.

specifications. Place one tablet in each of the 6 tubes of the basket. Add a disc to each tube and run the apparatus using pH 6.8 (simulated saliva fluid) maintained at 37±2^{0}C as the immersion liquid. The assembly should be raised and lowered between 30 cycles per minute in the pH 6.8 maintained at 37±2^{0}C. The time taken up by the tablet for complete disintegration with no palpable mass remaining in the apparatus was measured and recorded.

j) Mouth feel

To know mouth feel of the tablets, selected human volunteers were given placebo tablets and the taste sensation felt was evaluated.

k) In-vitro dissolution studies

In vitro release studies were carried out using tablet dissolution test apparatus USP XXIII. The following procedure was employed throughout the study to determine the *in-vitro* dissolution rate for all the formulations.

l) Accelerated Stability studies

The promising formulations (F4 and F5) were tested stability for a period of 3 months at accelerated conditions of a temperature 40^{0}C and a relative humidity of 75% RH, for their drug content.

RESULTS AND DISCUSSIONS

The FTIR spectrum of formulated blend showed characteristic peaks of drug which indicated that the compatibility of the drug with the excipients used. The spectrum was shown in Figure 1 and 2. The results obtained for angle of repose of the powdered blends was less than 30^0, the loose bulk density was ranged from 0.317±0.08 to 0.578±0.05 g/cm^3, the tapped bulk density was ranged from 0.358±0.01 to 0.711±0.11 g/cm^3, the percent compressibility was ranged from 12.12 to 22.50 %. All these values were represented in Table 2. The mean thickness values were found in the range from 2.95±0.15 to 3.25±0.08 mm, the hardness of formulated tablets was found to be 5.94±0.26 to 7.95±0.19 kg/cm^3. The loss in friability was ranged from 0.26±0.08 to 0.56±0.09 %. The Wetting Time was ranged from 92 ± 1.51 to 99 ± 1.47 sec, the disintegration Time was ranged from 22±8.26 to 39±2.32 sec. These values were represented in Table 3. The *in-vitro* dissolution profile of formulated tablets was shown in Figure 3. The dissolution parameters were shown in table 4. The comparative parameters of optimized formulations (F4 and F5) before and after the accelerated stability studies were shown in Table 5.

All the formulations showed angle of repose within 30^0 which indicates good flow. The values of loose bulk density and tapped bulk density help in calculating the % compressibility of the powder. All formulations show good compressibility. The formulated tablets were elegant and almost uniform thickness. All the formulations were almost uniform in specific method and possess good mechanical strength with sufficient hardness. The weight loss after friability test was found well within the approved range (<1%) in all the formulation, indicates the tablets possess good mechanical strength. All the tablets passed weight variation test as per the pharmacopoeial limits. All formulations showed quick wetting, this may be due to ability of swelling and also capacity of absorption of water. All superdisintegrants have high water absorption capacity and cause swelling. All formulations showed disintegration time less than 95 seconds, indicates the swelling of disintegration substance suggested mechanism of disintegration. The volunteers felt good taste in all the formulations. As the formulation was not bitter due to the presence of stevia leaf powder, which is 400 times sweeter than sucrose and the

Euginol in clove oil which acts as both flavoring and local anesthetic agent to block the sensation of taste buds. In oral disintegration all the formulations showed rapid disintegration in oral cavity. By observing the above results use of cross cormilose sodium and cross Povidone, in direct compression method results in hydrophilicity and swelling which in turn causes rapid disintegration. Thus these disintegrants are suitable in preparing the rapidly disintegrating tablets. This rapid dissolution might be due to fast breakdown of particles of superdisintegrants. In all formulations the drug release was nearer to 100% within 12 minutes. The optimized formulations F4 and F5 were selected for accelerated stability studies and the tablets possessed the same parameters even after the stressed conditions, indicates good stability properties of formulation.

Table 1: Composition of Mouth Dissolving Tablets of Metoclopramide Hydrochloride

Ingredients (mg)	Formulations				
	F1	F2	F3	F4	F5
Metoclopramide Hydrochloride	10	10	10	10	10
Mannitol	50	50	50	50	50
Cross carmellose sodium	10	20	30	40	50
Cross povidone	10	20	30	40	50
Stevia leaf Powder	5	5	5	5	5
Micro crystalline cellulose	304	284	264	244	224
Magnesium stearate	3	3	3	3	3
Talc	3	3	3	3	3
Clove oil (Flavoring agent and local anesthetic)	5	5	5	5	5
Total weight of the tablet 400mg					

Table 2: The physicochemical properties of granules

Formulation	Angle of Repose (θ)	Loose Bulk Density (g/cm^3)	Tapped Bulk Density (g/cm^3)	Compressibility (%)
F1	30.83±0.54	0.317±0.08	0.361±0.07	14.89±1.14
F2	29.98±0.51	0.555±0.52	0.711±0.11	22.50±1.11
F3	32.68 ±0.50	0.349±0.04	0.358±0.01	14.00±3.36
F4	28.20±1.54	0.577±0.03	0.645±0.03	12.35±0.25
F5	29.30±0.98	0.578±0.05	0.666±0.04	12.12±0.16

Table 3: Evaluation parameters of Tablets

Formulation	Thickness (mm)	Hardness (kg/cm^3)	Friability (%)	Wetting Time (sec)	Disintegration Time (sec)
F1	3.25±0.08	6.38±0.13	0.35±0.11	95±0.51	35±4.25
F2	3.02±0.05	6.10±0.17	0.56±0.09	92±1.51	39±2.32
F3	2.95±0.15	7.95±0.19	0.29±0.09	95±5.21	32±6.59
F4	3.06±0.01	6.95±0.51	0.26±0.08	99±1.47	22±8.26
F5	3.11±0.02	5.94±0.26	0.54±0.05	98±1.58	31±4.61
Number of trials (n) = 3					

Table 4: Tablet dissolution apparatus parameters

Parameter	value
Dissolution medium	900 ml of 0.1N HCl
Temperature	$37^0C \pm 1^0C$
RPM	50
Tablet taken	One tablet (Known drug content).
Volume withdrawn	5 ml every 2 minutes
Volume made up to	5 ml
λ_{max}	273 nm
Beer's range	1-10 µg/ml
Dilution factor	10

Table 5: Selected Formulations for Stability Studies F4 & F5 Stored at 40^0C/75% RH

Formulation	Tested after time (days)	Hardness (kg/cm^2)	Disintegration time (sec)	Wetting time (sec)	Friability (%)
F4	0	6.50±0.07	92±8.26	99± 1.47	0.34±0.06
	10	6.48±0.45	95±2.65	100± 2.55	0.36±0.02
	20	6.44±0.52	96±3.67	99± 1.89	0.38±0.03
	30	6.46±0.29	95±6.22	98± 2.29	0.37±0.01
F5	0	6.48±0.04	51±4.61	98± 1.58	0.67±0.01
	10	6.35±0.31	53±5.48	102± 2.54	0.65±0.02
	20	6.39±0.55	54±3.67	101± 3.25	0.69±0.05
	30	6.42±0.15	52±4.98	100± 4.52	0.68±0.06

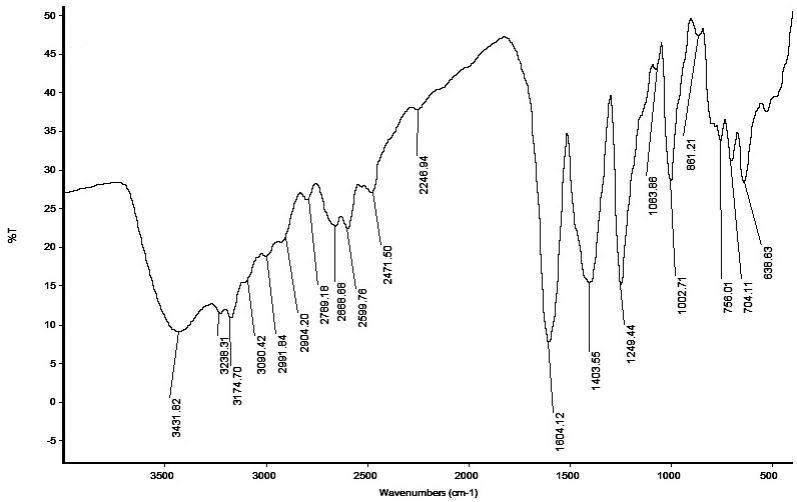

Figure 1: FTIR spectrum of Metoclopramide Hydrochloride

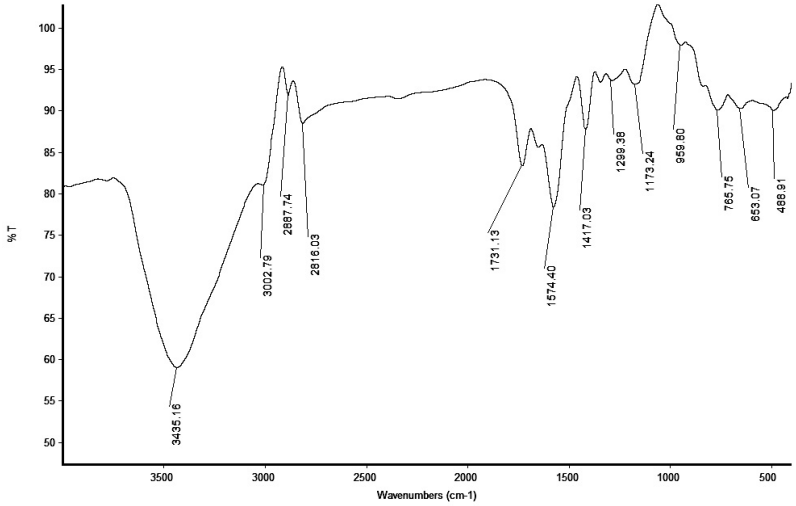

Figure 2: FTIR spectrum of formulation blend (F5)

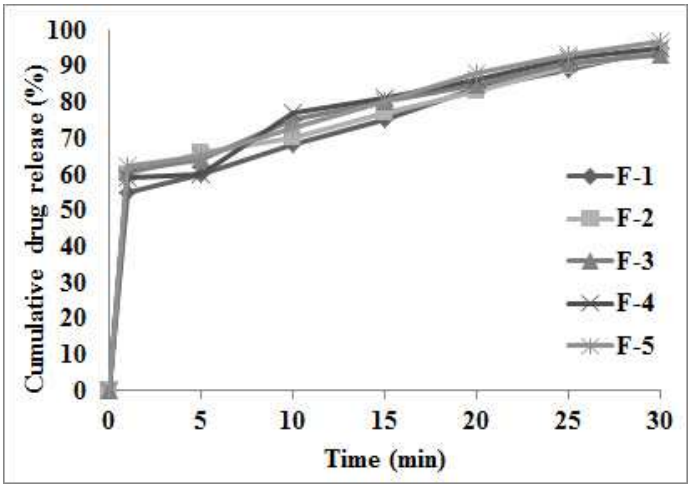

Figure 3: *In-vitro* drug release profile of formulated tablets

REFERENCES

[1] Biradar SS, Bhagavati ST, Kuppasad IJ., *The Int. J. Pharmacol*;4(2): **2006**, 1531-2976.
[2] Kaushik D, Dureja H, Saini TR., *Indian Drugs*-Bombay; 41:**2004**, 187-93.
[3] Seager H., *J Pharm Pharmacol*; 50: **1998**, 375-8.
[4] Swann IL, Thompson EN, Qureshi K., *British medical journal* 2 (6199): **1979**, 1188.
[5] Shindler JS, Finnerty GT, Towlson K, Dolan AL, Davies CL, Parkes JD., *British journal of clinical pharmacology* 18 (6): **1984**, 959–62.
[6] Rossi S, editor. Australian Medicines Handbook 2006. Adelaide: Australian Medicines Handbook; **2006**.
[7] Silvers D, Kipnes M, Broadstone V, et al. *Clinical therapeutics* 20 (3): **1998**, 438–53.
[8] Sharma S, Gupta GD., *AJP;*2: **2008**, 70-2.
[9] Kuchekar B.S., Badhan A.C.and Mahajan H.S., *Pharma Times*,35, **2003**, 7-9.
[10] Avari, N.G. and Bhalekar, M. Cation., *Indian Drugs*, 41, 1, **2004**, 19-23.
[11] United State Pharmacopoeia 24/NF 19, Asian Edition. The Official compendia of Standards, United States Pharmacopoeial Convection Inc. Rockville, **2000**, 1913-1914.
[12] Remunan C, Bretal M, Nunez A, Bila Jato JL. *Int J Pharm*; 80: **1992**, 151-159.