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Formulation and evaluation of mouth dissolving tablets of Dicyclomine HCl with enhanced bioavailability

Gupta S.C.*, Gurjar R., Khambete H., C K Sudhakar., Jain S.

Department of Pharmaceutics, Smriti College of Pharmaceutical Education, Indore

ABSTRACT

Dicyclomine HCL is an antispasmodic drug which is widely used in treatment of smooth muscle spasm of the gastrointestinal tract but it undergoes to first pass Metabolism. So that to develop mouth-dissolving tablet of Dicyclomine HCL to avoid first pass metabolism and increase bioavailability. This offers a new range of product having desired characteristics and intended benefits. In this study, the mouth dissolving tablets were prepared using direct compression method. Tablets produced by direct compression method contain D-Mannitol as diluent, crospovidone as a superdisintegrant and aspartame as a sweetener. The dissolution study was performed on PBS 6.8 (salivary pH) and the In-vitro release was found 99.80% without leaving residue for F6 Batch. Moreover the drug release was found to be comparable to the marketed tablet.

Key Words: Dicyclomine HCl, Mouth-dissolving tablet, direct compression method.

INTRODUCTION

The concept of Mouth dissolving Drug Delivery System emerged from the desire to provide patient with more conventional means of taking their medication. It is difficult for many patients to swallow tablets and hard gelatin capsules. Hence they do not comply with prescription, which results in high incidence of non-compliance and ineffective therapy. A mouth-dissolving drug delivery system, in most cases, is a tablet that dissolves or disintegrants in the oral cavity without the need of water or chewing. These are also called melt-in-mouth tablets, repimelts, spongy tablets, orzo-dispersible, quick dissolving or rapid disintegrating tablets. It would, therefore, be advantageous for administration to the patients who cannot swallow, such as the elderly, stroke victims, bedridden patients and who refuse to swallow, such

as pediatric, geriatric & psychiatric patients with improved compliance and Good mouth feel property. Particularly the difficulty is experienced by pediatric and geriatric patients. Such problems can be resolved by means of Mouth Dissolving Tablet, When put on tongue, this tablet disintegrates instantaneously, releasing the drug, which dissolves or disperses in the saliva. Some drugs are absorbed from the mouth, pharynx and esophagus as the saliva passes down into the stomach. In such cases, bioavailability of drug is significantly greater than those observed from conventional tablet dosage form Mouth-dissolving drug delivery systems have rapidly gained acceptance as an important new way of administering drugs. There are multiple mouth-dissolving OTC and Rx products on the market worldwide, most of which have been launched in the past 3 to 4 years. There have also been noteworthy increases in the number of new chemical entities under development using a mouth-dissolving drug delivery technology. Pharmaceutical marketing and pharmaceutical manufacturers to develop a given drug entity in a new and improved dosage form. A new dosage form allows a manufacturer to extend market exclusivity, while offering its patient population a more convenient dosage form. [1-3]

Various techniques can be used to formulate Mouth dissolving tablets. Direct compression one of the techniques requires the incorporation of a super disintegrants into the formulation the use or highly water soluble excipients to achieve fast tablet disintegration. [18-20] Direct compression does not require the use of water or heat during the formulation procedure and is the ideal method for moisture and heat-labile medications. Some drugs are absorbed from the mouth, pharynx and esophagus as the saliva passes down into the stomach. In such cases, bioavailability of drug is significantly greater than those observed from conventional tablet dosage form.

The aim of purpose work was to formulate and characterization mouth dissolving tablets of Dicyclomine Hydrochloride for rapid dissolution of drug and absorption, which may produce the rapid onset of action in the treatment of smooth muscle spasm of the gastrointestinal tract .

EXPERIMENTAL SECTION

Dicyclomine HCl was procured as a gift sample from Healthy Life Pharma Ltd, Mumbai (Maharashtra). Aspartame was procured as a gift sample from Cadilla Pharmaceuticals, Ahmadabad (Gujarat). Microcrystalline cellulose (Avicel PH 102, and Avicel PH 101), Mannitol SD 200, Crospovidone (Polyplasdone XL), Sodium Starch Glycolate (Primogel), Cros carmellose sodium (Ac-Di-Sol), Magnesium stearate and Talc are purchased from Loba Chemicals.

Preparation of Mouth-dissolving tablet:

Tablets containing Dicyclomine HCl were prepared by direct compression method. Tablets are compressed directly from powder blends of active ingredient and suitable excipients (including fillers, disintegrants, and lubricants). Drug, directly compressible Mannitol, Superdisintegrant (Sodium starch glycolate, Ac-Di-Sol and Cros povidone), Microcrystalline Cellulose PH 102, Aspartame, Vanilla flavor and Talc were mixed together for 20 min. Magnesium stearate, was then added and mixed for 5 min. The powder blend was compressed into the tablets on tablet punching - machine.

Table 1: Composition of different batches of mouth-dissolving tablets of Dicyclomine Hydrochloride

INGREDIENTS	F1	F2	F3	F4	F5	F6
Dicyclomine Hydrochloride	20	20	20	20	20	20
D-Mannitol	199	199	199	199	199	199
Microcrystalline cellulose	102.32	100.32	102.32	100.32	102.32	100.32
Ac-Di-Sol	10	12	-	-	-	-
Sodium starch glycolate	-	-	10	12	-	-
Cros povidone	-	-	-	-	10	12
Aspartame	15	15	15	15	15	15
Vanilla Flavor	2	2	2	2	2	2
Magnesium stearate	1	1	1	1	1	1
Talc	1	1	1	1	1	1
Total	**350**	**350**	**350**	**350**	**350**	**350**

Evaluation of mouth dissolving tablet: The formulated mouth dissolving tablets were evaluated for different parameters like general characteristic, uniformity of weight, hardness, wetting time, uniformity of dispersion, disintegration test and drug release profile.

Weight variation test:
Twenty tablets were taken and their weight was determined individually and collectively on a digital weighting balance. The average weight of one tablet was determined from the collective weight.

Hardness: Hardness in simple term is the property of material by which it is able to hold all its constituents in an intact form. Hardness is amount of strength of tablet to withstand mechanical shocks of handling in manufacture, packaging and shipping and tablet should be able to withstand reasonable abuse when in the hand of consumer .The hardness of tablet is evaluated by Monsanto hardness tester or Pfizer tester**.** The hardness is measured in kg/cm^2**.** [1-2]

Friability: Friability is also mechanical strength of tablet. It is evaluated by Roche Friabilator with 100 revolution rotating 25 per minute for 4 min by using 6 tablets. According to USP tablets should have limit < 1% for acceptance. [1,2,5,8]

$$\% \text{ Friability} = \frac{(\text{Wt. of 20 tablets before rotation} - \text{Wt. of 20 tablets after rotation}) \times 100}{\text{Wt. of 20 tablets before rotation}}$$

Drug content: Prepare the composite specimen of a sufficient number of tablets. All the tablet are weighed and triturated in pestle-mortar .then calculate the weight of one individual tablet (one dosage unit) weight and then follow the given assay procedure in Individual Monograph. Absorbance will be taken at λ_{max} against the blank and concentration of drug is determined by using standard equation. [5]

Wetting time: Wetting time of the mouth dissolving tablet is another important parameter, which needs to be assessed to give an insight into the disintegration properties of the tablets; a lower wetting time implies a quicker disintegration of the tablet. This method will duplicate the *in vivo* disintegration, as the tablet is motionless on the tounge. Five circular tissue papers of 10

cm diameter were placed in a petri dish with a 10cm diameter. Ten millimeters of water-containing methyl red, a water-soluble dye, was added to Petri dish. A tablet was carefully placed on the surface of the tissue paper. The time required for water to reach upper surface of the tablet was noted as a wetting time. [20]

***In vitro* disintegration time:** The disintegration test was performed using an USP disintegration apparatus, with distilled water at 37±0.5^{0}C. The time reported to obtain complete disintegration of six tablets were recorded and average was reported. [5]

***In vitro* dissolution testing:** Dissolution study was conducted for all the formulation using USP type-II apparatus. The release study was carried out in USP Type 2 dissolution apparatus containing 900ml 6.8 pH phosphate buffers at 50 rpm and 37˚C temperature.[8,21,22]

Table 2: Evaluation parameters of prepared tablets Mouth Dissolving Tablet of Dicyclomine Hydrochloride

S.No.	Batch codes	Weight variation	Hardness (kg/cm^2)	% Friability	Average disintegration time (sec)	Average wetting time (sec)	% drug content
1	**F1**	3.23±0.20	3.23±0.20	0.75±0.02	22.00±4.39	41.66±3.39	96.22±1.27
2	**F2**	2.66±0.23	2.90±0.29	0.75±0.03	18.00±4.96	41.66±2.49	97.15±1.47
3	**F3**	3±0.40	1.83±0.23	1.46±0.18	18.00±4.61	48.00±2.44	95.98±0.79
4	**F4**	2.83±0.23	3.00±0.40	0.91±0.02	21.50±3.10	65.00±2.44	95.65±0.66
5	**F5**	3.41±0.49	2.83±0.23	1.5±0.02	20.00±5.09	47.66±2.05	96.47±2.03
6	**F6**	3.56±0.23	3.33±0.23	0.69±0.02	22.75±2.98	50.33±1.24	96.83±0.37

Figure1. Photographs of Dicyclomine HCl Mouth dissolving tablet

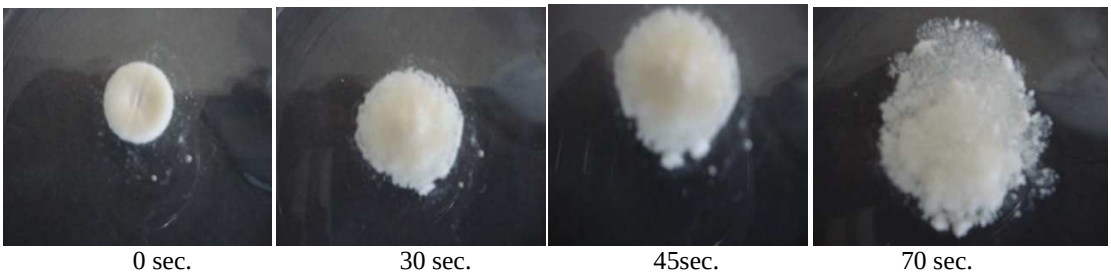

Figure2. Photographs of Wetting time Dicyclomine HCl Mouth dissolving tablet

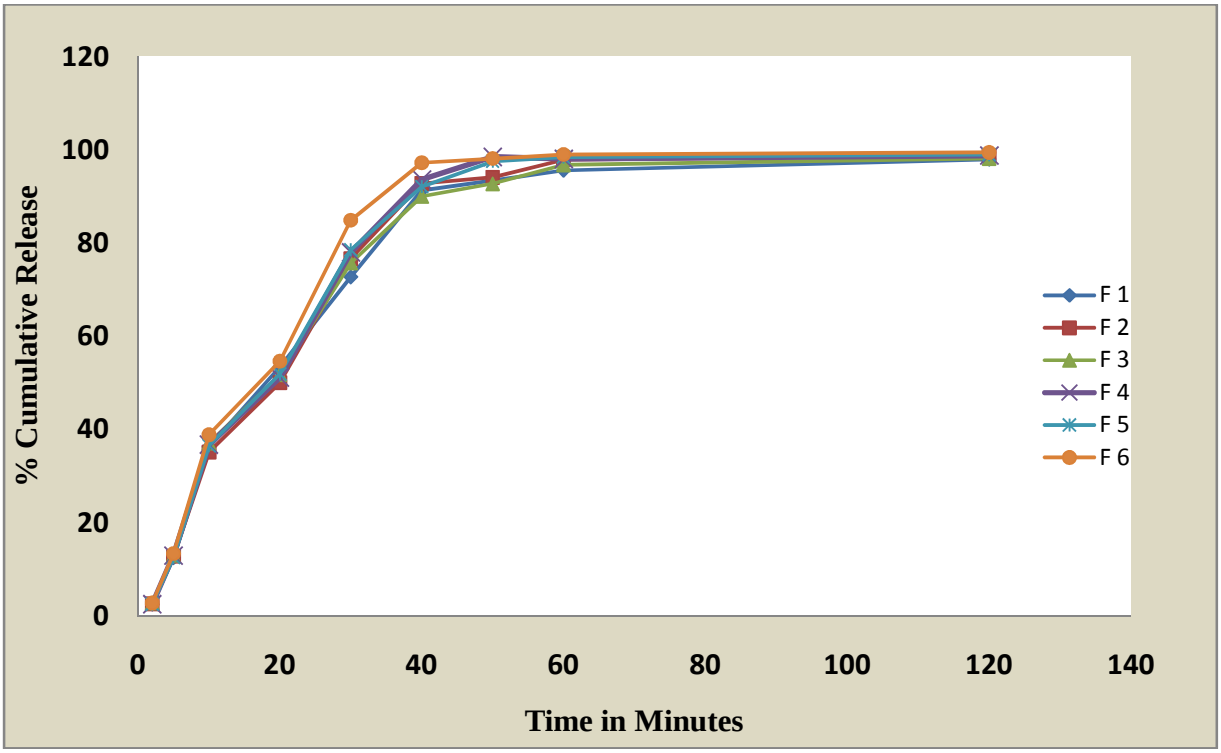

Figure 3: % Cumulative Release of All batches of Dicyclomine HCl Mouth dissolving tablets

RESULTS AND CONCLUSION

Mouth Dissolving tablets of Dicyclomine Hydrochloride were prepared by super disintegrants addition method and evaluated for various evaluation parameters of the tablets. Total Six formulations were designed. The hardness of tablets from all formulations was in between 1.83 to 3.36 kg/cm^2. All the formulations showed friability below 0.9 %. All the tablets were found to pass the uniformity of weight. Content of Dicyclomine Hydrochloride from all formulation was found in range of 94.09% to 97.15%. All the formulations tablets disintegrate in 18 to 22 sec respectively. The wetting time was measured and found in range of 41.66 to 65.00 sec.

Super disintegrants Polyplasdon XL (Crospovidone) batch no. **F 6** displays best results among six batch of the Mouth Dissolving Tablet. The *in-vitro* release study was carried out using 900 ml of 6.8 pH phosphate buffer as dissolution medium at 50 rpm using USP dissolution apparatus. Formulation F 6 showed rapid dissolution and cumulative drug release at the end of 40 min. was more than 97% in 6.8pH phosphate buffer.

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