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FORMULATION AND EVALUATION OF EFFERVESCENT TABLETS OF METFORMIN HYDROCHORIDE

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ABSTRACT

Recently, fast dissolving drug delivery systems have started gaining popularity and acceptance as new drug delivery systems, because they are easy to administer and lead to better patient compliance. Usually, Metformin hydrochloride is to reduce glucose absorption intestinally into the systemic circulation, to decrease glucose synthesis in liver, and to increase up take of glucose into the tissues. These formulations were subjected to various evaluation parameters like hardness, friability, drug content, in-vitro release studies drug and polymer interaction . Aim of this study was to formulate Effervescent tablet with sufficient mechanical integrity and to achieve faster disintegration in the water. They are intended to be dissolved or dispersed in water before use. Effervescent compositions in the form of tablets comprising a therapeutic agent, a granulating agent, a micro particulate effervescent component and an effervescent system which dissolve rapidly in water to yield an effervescent solution containing a completely dissolved therapeutic agent and a process for their preparation.

Key words: Effervescent Tablets, Metformin hydrochloride, Reduce glucose absorption

1. INTRODUCTION

The As per revised definition proposed to US FDA "Effervescent tablet is a tablet intended to be dissolved or dispersed in water before administration" It generally contains in addition to active ingredients, mixture of acids/acid salts (citric, tartaric, malic acid or any other suitable acid or acid anhydride) and carbonate and hydrogen carbonates (sodium, potassium or any other suitable alkali metal carbonate or hydrogen carbonate) which release carbon dioxide when mixed with water. Occasionally, active ingredient itself could act as the acid or alkali metal compound necessary for effervescent reaction. Effervescent tablets are uncoated tablets that generally contain acid substances and carbonates or bicarbonates and which react rapidly in the presence of water by releasing carbon dioxide. Effervescent tablets are uncoated tablets that generally contain acid substances and carbonates or bicarbonates and which react rapidly in the presence of water by releasing carbon dioxide [1]. Oral route is the preferred rout of administration of drug because of low cost of therapy and ease of administration more of patient compliance [2]. Effervescent is formation of gas bubbles that rise to the surface of a fluid, rising in little bubbles of gas, boiling or bubbling from the release of gas [3, 20]. Effervesent tablets are designed to produce a solution rapidly with the simultaneous release of carbon dioxide. When such a tablet is dropped into a glass of water, a chemical reaction is initiated between the acid and sodium bicarbonate to from the sodium salt of the acid, and produce carbon dioxide and water. The reaction is quite rapid and is usually completed within one minute or less [10]. In Oral Drug Delivery System to Floating drug delivery systems were first described by Davis in 1968. Metformin reduces hepatic glucose output, largely by inhibiting hepatic gluconeogenesis[21]. Metformin (Antidiabetic) is now believed to become the most widely prescribed anti-diabetic drug in the world and about 42 million prescriptions are being generated in United States on regular basis (Bailey and Day, 2004). Moreover, the percentage of patients suffering from type 2 diabetes is elderly people, showing dysphasia. The problem becomes even more severe due to big tablets (high dose 500- 1000mg) having a size of 19mm × 10.5mm and need for daily intake of drug [4]. Metformin, the only currently available biguanide, is clssed as an insulin sensitizer, that is, it increase glucose uptake and utilization by target tissue, thereby decreasing insulin resistance. Metformin reduces hepatic glucose output, largely by inhibiting hepatic gluconeogenesis, it also slow intestinal absorption of sugars. Metformin is well absorbed orally [17].

2.MATERIALS AND METHODS [4, 5, 6, 7,]

Metformin hydrochloride, Citric acid, Tartaric acid, Sodium carbonate, Pottasium carbonate, Manitol, Sorbitol, Polyvinyl pyrolidone (PVP), Polyethylglycone (PEG), Sweetner(saccharine) and The drug-polymer interactions were studied

by IR spectrometer from Choksi Laboratories, Indore, Registration No. AABCC2523LST004. All other chemicals used were of analytical reagent grade. Double distilled water was used in entire study.

2.1.Preparation of Floating Tablets of Metformin Hydrochloride: [8, 9, 10, 11, 12]

Effervescent tablets of Metformin hydrochloride were prepared by direct compression technique. All the ingredients were accurately weighed and passed through sieves No 44# and in order to mixed the ingredients properly. Drug and different concentration of Sodium bicarbonate, Citric acid, Talc and Magnesium stearate, Pottasium carbonate, Manitol, sorbitol, Sweetner (saccharine) Polymer were blend in mortar followed by the addition of Polyvinyl pyrolidone (PVP), Polyethylglycone (PEG),. After thoroughly mixing the ingredients tablets were compressed in rotary punching machine. Effervescent tablets of Metformin Hydrochloride were prepared by direct compression technique.

3.RESULT AND DISCUSSION

3.1. Pre-Compression Parameters [8, 18]

a)Angle of repose (θ): The values obtained for angle of repose for all formulations were tabulated in Table 2. The values were found to be in the range from 24°.12' to 28°.20'. This indicates good flow property of the powder blend for direct compression.

b)Compressibility index: The values obtained for Compressibility index for all formulations were tabulated in Table 2. Compressibility index value ranges between 12.16 to 18.30 % indicating that the powder blend have the required flow property.

3.2. Post Compression Parameters

a)Shape of the tablet: Microscopic examination of tablets from each formulation batch showed circular shape with no cracks [9].

b)Thickness: The dimensions determined for formulated tablets were tabulated in Table 3. Tablets mean thickness were almost uniform in all the ten formulations and were found to be in the range of 3.15 mm to 4.91 mm [8, 9].

c)Hardness test: The dimensions determined for formulated tablets were tabulated in Table 3. The measured hardness of tablets of each batch ranged between 3.03 – 4.74 kg/cm2. This ensures good handling characteristics of all batches [12].

d)Friability test: The values of friability test were tabulated in Table 3. The % friability was less than 1% in all the formulations ensuring that the tablets were mechanically stable [14, 15, and 16].

e)Weight variation test: The percentage weight variations for all formulations were shown in Table 3. All the tablets passed weight variation test as the % weight variation was within the Pharmacopoeial limits of ±5% of the weight. The Weight variation of tablets of each batch ranged between 985.95 – 962.88 mg [8, 9, 10, 12, and 13].

f)Disintegration time: Place one tablet in a 250-ml beaker containing water at 20º to 30º; numerous gas bubbles are evolved. The values of Disintegration test were tabulated in Table 3 [19].

g)In-vitro Dissolution study: The plot of cumulative percentage drug release versus time (min) was plotted and depicted as shown in Table 4. From the in vitro dissolution data it was found that formulation MET-8 containing PVP and Sorbitol absent released 100.2 % of drug within 5 min. [1, 17]

h)Compatibility Studies: Compatibility studies were performed using IR spectrophotometer and the IR spectrum of the obtained pure drug and formulation MET-8 were studied. The characteristic absorption peaks of pure Metformin and MET-8 obtained show in table No. 5, 6 [5, 22, 23, 24, 25,26,27,28, and 29].

4.CONCLUSION

The Study Was Under with an aim to formulate effervescent tablet of Metformin Hydrochloride act by reducing production of reducing of glucose absorption which involved in decrease glucose synthesis in liver. In present work an attempt has been made to formulate an effervescent tablet containing immediate release Metformin Hydrochloride using acid and bases. The effervescent tablets Metformin Hydrochloride were prepared direct compression. The prepared tablets were evaluated for content uniformity and physical parameters. Capping and sticking problem were observed, different formulation contain of PVP and sorbitol direct compression the powder become free flowing so good. At the time of manufacturing of effervescent tablet humidity and temperature should be maintained, strictly.The effervescent tablets were formulated using different acid and bases. In direct compression method used PVP as adhesives, potassium carbonate as a disintegration and Manitol to act diluents. There are nine formulations that contain the Citric acid; Tartaric acid and Sodium carbonate were formulated. These nine formulations were evaluated for hardness, friability, and weight variation, effervescent time. From the above summary it was concluded that, the effervescent tablets of Metformin Hydrochloride can be formulated for quick Antidiabetic by effervescence reaction using Citric acid (18.75%), Tartaric acid (18.75%), and Sodium carbonate (9.37%), Potassium carbonate (9.37%) as the disintegration gives the better effervescent. The PVP (4.68%) used as binding, Manitol (4.68%) as the act bulking and diluents, Talk (3.64%) as lubricant agent.

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Table 1: Table 1: Composition of all the formulations (Formulations MET -1 – MET -9)

Ingredients (Mg per tablet)	MET-1 (mg)	MET-2 (mg)	MET-3 (mg)	MET-4 (mg)	MET-5 (mg)	MET-6 (mg)	MET-7 (mg)	MET-8 (mg)	MET-9 (mg)
Metformin Hydrochloride	250	250	250	250	250	250	250	250	250
Citric acid	150	200	300	350	100	50	_	180	360
Tartaric acid	210	160	60	10	260	310	360	180	_
Sodium carbonate,	50	60	70	130	120	70	_	90	180
Pottasium carbonate	130	120	110	50	60	110	180	90	_
Manitol	-	30	40	-	40	50	_	45	90
Sorbitol	-	15	50	-	5	40	_	_	_
Polyvinyl pyrolidone	40	30	-	50	40	-	90	45	_
Polyethylglycole	50	15	-	40	5	-	_	_	_
Talc	35	35	35	35	35	35	35	35	35
Magnesium state	35	35	35	35	35	35	35	35	35
Sweetener (saccharine)	10	10	10	10	10	10	10	10	10
Total Weight	**960**	**960**	**960**	**960**	**960**	**960**	**960**	**960**	**960**

Table 2: Pre-compression parameters of MET-1 to MET-9

Formulation	Angle of Repose (θ)	Compressibility Index (%)
Met-1	26°.01'	15.20
Met-2	25°.62'	18.30
Met-3	24°.12'	13.25
Met-4	28°.01'	16.02
Met-5	26°.'65	14.87
Met-6	28°.20'	12.16

Met-7	27°.41'	12.25
Met-8	26°.65'	14.10
Met-9	28°.11'	12.71

Table 3: Thickness, Hardness**,** Friability**,** Variation and disintegration of MET-1 to MET-9

Formulation	Thickness (mm)	Hardness (Kg/cm^2)	Friability (%)	Weight Variation (mg)	Disintegration (sec)
Weight					
MET-1	4.12	4.03	Pass	960.33	125
MET-2	4.41	4.47	Pass	962.88	Fail
MET-3	3.01	4.74	Fail	960.83	141
MET-4	4.01	3.03	Pass	959.54	140
MET-5	3.85	3.69	Fail	961.10	Fail
MET-6	3.12	3.88	Fail	958.95	185
MET-7	4.91	3.54	Pass	960.80	125
MET-8	3.40	4.69	Pass	960.50	195
MET-9	3.15	4.12	Fail	959.51	180

Table 4: *In vitro* Dissolution study of Effervescent Tablet (MET-8)

Time(min)	Absorbance	Concentration (µg/ml)	Amount present in 900 ml (mg)	% Drug release
1	0.412	0.0512	184.08	73.72
2	0.510	0.0629	226.0	90.4
3	0.550	0.0690	248.4	99.4
4	0.551	0.0696	250.56	100.2
5	0.551	0.0696	250.56	100.2

Table-5: IR Frequency (cm^{-1}) of pure Metformin

Formula code	Group / Vibration	Frequency (cm^{-1})
Pure Metfomin Hydrochloride	Chlorine (Cl) Stretching	
	(C-Cl)	794.61
	Amines (NH_2) Stretching	
	(N-H)	3147.6
	Alkynes (CH_3) Stretching	
	C-H	3147.6
	C-C	1056.91

Table-6: IR Frequency (cm^{-1}) of MET-8

Formula code	Group /Vibration	Frequency (cm^{-1})
MET-8	Chlorine (Cl) Stretching	
	(C-Cl)	786.9
	Amines (NH_2) Stretching	
	(N-H)	3317.32
	Alkynes (CH_3) Stretching	
	C-H	2962.44
	C-C	1064.63

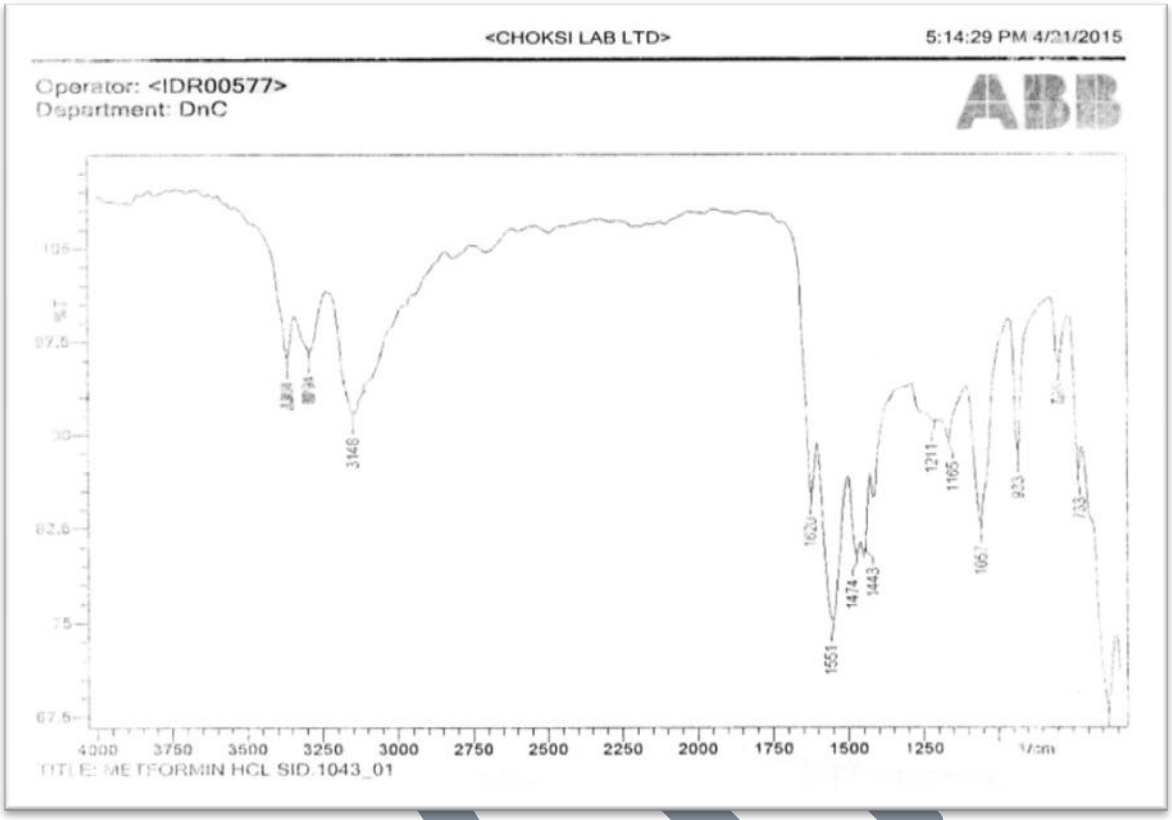

Figure 1: IR spectra of Metformin HCL

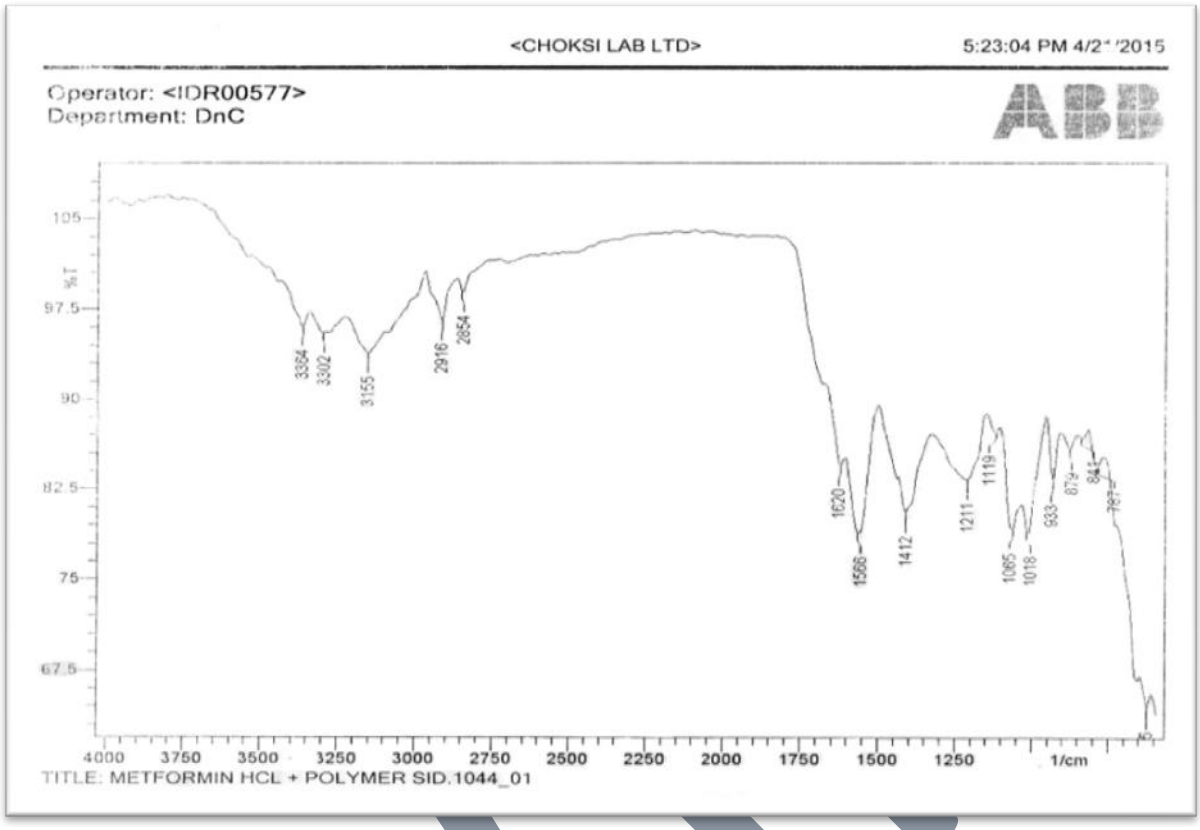

Figure 2: IR spectra of Metformin HCL + Polymers

Table-9: Parameter of formula No. MET-8

Parameter	MET-8
Disintegration Time (sec)	195
% drug release within 1 min	73.72