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REVIEW ON -Formulation and Evaluation of Mouth Dissolving Olmesartan Medoxomil Tablet.

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Abstract: The goal of this study is to create a mouth-dispersible tablet of the hypertension medication Olmesartan medoxomil. Olmesartan medoxomil mouth dissolving pills were made with three different superdisintegrants: crospovidone, sodium starch glycolate, and cross-carmellose sodium. The approach .The direct compression method of tablet manufacturing is assessed for physicochemical evaluation parameters, including weight variation, hardness, friability, uniformity of drug content, water absorption ratio, wetting time, invitrodisintegration time, and in-vitro dissolution studies.It was demonstrated in this study that formulations containing crospovidone out performed other formulations in terms of in-vitro findings. Nonetheless, formulations with an 8% w/w concentration of any superdisintegrants have demonstrated superior optimal outcomes.

Keywords - Fast dissolving tablet, Olmesartan medoxomil, In- vitro drug release , Superdisintegrant

I. INTRODUCTION

High blood pressure is one of the main risk factors that are causing as increase in cardiovascular disease related morbidity and health worldwide along with smoking hypercholesteremia , and hypoglycemia. Now a day fast dissolving tablets are gaining more importance in the market. Currently these tablets are available in the market for treating many disease conditions. More is concern is on hypertension ,migraine, dysphasia, nausea and vomiting, Parkinson's disease, schizophrenia, pediatric emergency(1-4) After oral administration the inert prodrug Olmesartan medoxomil is quickly absorbed and quickly de esterifies in the gastrointestinal tract producing active metabolite Olmesartan. For rapid onset of pharmacological effect from drugs, especially in the treatment of acute disorders, we preferred parenteral administration, but this method may not always be convenient for the patient. Therefore, there is growing interest in developing new, non-parenteral, reliable and convenient dosage forms using administration routes where a rapidly dissolved drug is immediately absorbed into the systemic circulation. Tablet formulations are generally the first choice for drug administration because of the relative ease of both production and usage. However, for acute disorders, the time to onset of action for a conventional oral tablet is generally not acceptable; this is usually attributable to gastric emptying causing a highly variable lag time between drug administration and onset of intestinal absorption(5) these tablet will give the active ingridients a high dissolution rate of dissolution increasing in bioavailability. The patient with above conditions show convenience with fast dissolving tablets over conventional tablets because of ease of administration, swallowing, pleasant taste and availability in several flavors(6) steady and having an easy time passing through the administration site's mucosal barrier. Moreover, the dosage form must dissolve quickly at the administration site while maintaining a long enough contact time. A portion of the dosage will not be absorbed through the oral route if the medication dissolves completely, the contact time is brief, or the penetration is too low. mucosa and will be ingested, which will impact bioavailability afterwards .Saliva swiftly enters the tablet pores when mouth dissolving tablets are held in

the oral cavity, hastening the disintegration process . The fundamental method utilized in the creation of mouth-dispersing tablets is the application of superdisintegrants, which offer instantaneous tablet disintegration upon application to the tongue, releasing the medication into saliva. In these situations, bioavailability. Drug delivery via the oral mucosa is a promising route, when one wishes to achieve a rapid onset of action or improved bioavailability for drugs with high first-pass metabolism [7]

II. MATERIALS AND METHODS

Olmesartan medoxomil was obtained from gift sample, glenmark Mumbai, sodium starch glycolate and microcrystalline cellulose , croscarmellose sodium obtained from molychem Mumbai, Crosspovidone, Mannitol, Lactose, Talc and Magnesium stearate were obtained from S.D. Fine Chemicals. Pvt Ltd, Mumbai, India. All chemicals and solvents used were of analytical grade.

Formulation of mouth dissolving tablets :

Dissolving tablets of olemesartan medoxomil mouth were made by the direct compression method with various excipients. Microcrystalline cellulose, lactose, sodium starch glycolate, mannitol, and croscarmellose sodium were the excipients utilized. The formulas' compositions are displayed in Table 01. Every component of the mouth Olmesartan medoxomil dissolving pills were weighed and combined in a mortar using a pestle and mortar. Then, using a Rimek MINI PRESS-I MT tablet machine, the blended substance was softly squeezed on the 8mm flat-biconvex punch. The formulation's overall weight was kept to 200 mg. A hardness adjustment of 2-4 kg/cm2 was made.

MANUFACTURING OF TABLETS DIRECT COMPRESSION:

Table no.1 composition of mouth dissolving tablets

Name of ingridients	F1	F2	F3	F4	F5	F6	F7	F8	F9
Olmesartan	20	20	20	20	20	20	20	20	20
CCS	-	-	-	6	8	10	-	-	-
SSG	6	8	10	-	-	-	-	-	-
Crosspovidone	-	-	-				6	8	10
Microcrystalline cellulose	50	50	50	50	50	50	50	50	50
Lactose monohydrate	102	100	100	102	100	100	102	100	100

Mannitol	**10**	**10**	**8**	**10**	**10**	**8**	**10**	**10**	**8**
Magnesium stearate	**2**	**2**	**2**	**2**	**2**	**2**	**2**	**2**	**2**
Talc	**10**	**10**	**10**	**10**	**10**	**10**	**10**	**10**	**8**
Total	**200**	**200**	**200**	**200**	**200**	**200**	**200**	**200**	**200**

III. EVALUATION OF BLEND

The powder blend was evaluated for follow pre-compresion parameters..

Precompression parameters :

7.4.1 Derived characteristics

Preformulation testing examines the physical and chemical characteristics of medicinal ingredients both by themselves and in combination with excipients. It is the initial phase in the methodical creation of dosage forms. The Preformulation testing's main goal is to produce data that will assist the formulation in creating a stable and bioavailable dosage form.

7.4.2 Angle of repose

A vertically adjustable funnel was used to pour the mixture through until the desired maximum cone height (h) was reached. The following formula was used to measure the heap's radius (r) and determine the angle of repose.

$\tan \theta = h/r$

Consequently, $\theta = \tan^{-1}(h/r)$.

In this case, θ stands for angle of repose,

h for cone height,

r for base radius of the cone.

Table no.2 Correlation between angle of repose and flow property

Sr.no	Angle of repose	Flow property
1	**<20**	**Excellent**
2	**20-30**	**Good**
3	**30-40**	**Passable**
4	**>34**	**Very poor**

Bulk Density

By carefully pouring 2 grams of the drug sample via a glass funnel into a 10 milliliter dry graduated measuring cylinder, the bulk density of the medication was ascertained. The sample's occupied volumes were noted. The bulk density was calculated.

Bulk density(g/ml) = weight of sample in gram / volume occupied by sample

Tapped density

By carefully pouring 5 grams of sample through a glass funnel into a 10 milliliter dry graduated measuring cylinder, the tapped density of the medication was ascertained. From a height of two inches, the cylinder was tapped until the volume remained constant. was acquired. After tapping, the sample's volume was measured, and the tapped density was computed.

Tapped density(g/ml) = weight of sample in gm/volume occupied by the sample.

Compressibility index:

Comparing the bulk and tapped densities of a powder is another easy way to assess its flow properties; Carr's compressibility provides a helpful empirical reference.

$$\text{Carrs index} = \frac{\text{Tapped density} - \text{Bulk density}}{\text{Tapped density}} \times 100$$

IV. Evaluation of mouth dissolving tablet:

The physiological characteristics of the prepare mouth dissolving tablet , such as weight variation, hardness, thickness, friability , and drug content, were assessed.

In vitro disintegration time :

using a tablet , the disintegration time of the tablet was calculated in accordance with the Indian pharmacopieal monograph**.**

Wetting time :

time Five circular tissue paper of 10 cm diameter were placed in a Petri dish. 10 ml of simulated saliva pH (pH 6.8phosphate buffer) was poured into the tissue paper placed in the Petri dish. Few drops of eosin solution were added to the Petri dish. A tablet was placed carefully on the surface of the tissue paper. The time required for the solution to reach upper surface of the tablet was noted as the wetting **[8].**

In vitro drug release study

The drug release rate from mouth dissolving tablets was studied using the USP type II dissolution test apparatus. The dissolution test was performed using 900 ml of phosphate buffer (pH 6.8) as the dissolution medium at 50 rpm and 37 ± 0.5˚C. 5 ml of aliquots were periodically withdrawn and the sample volume was replaced with an equal volume of fresh dissolution medium. The samples were analyzed spectrophotometrically at 250 nm[9]

In vitro Dispersion time test

To evaluate in vitro dispersion time, a tablet was dropped into a beaker contains 50 ml of Ph 6.8 Buffer. For each formulation , three tablets were choosen at random, and an in vitro dispersion time measurement was made

Uniformity of content

20 pills were broken up into a powder that contained 20 mg of olemesartan medoxomil. This powder was t hen dissolved in 100 millilitres of phosphate buffer, mixed, and filtered.Using phosphate buffer pH 6.8, 1 millilitre of the solution was diluted to 10 millilitres, and a UV Spectrophotometer was usedo measure the absorbance at 257 nm.Using UV spectroscopy, the quantity of medication in each formulation was ascerta ined.

water absorption Ratio (25)

A small piece of tissue paper folded twice was placed in a small petridish containing 6ml of water. A tablet was put on the paper and the time required for complete wetting was measured. The wetted tablet was then reweighed. Water absorption ratio, R was determined by using following formula were given

$$R = \frac{Wa - Wb}{Wb} \times 100$$ Where

, Wa=The weight of tablet after water absorption,

Wb=The weight of tablet before water absorption.

V. RESULT AND DISCUSSION:

The angle of repose were measured are determined to be between 280.50 and 310.87 degrees, showing good flow characteristics. The compressibility index values were discovered to be between 18 and 20%.This suggests the flow that is passable. Mass variation were within the 10% hence the fluctuation is within tolerance . Good flow was found is in the precompression study overall.and the powdered blends compression characteristics.The weight fluctuation was discovered to be within the 10% tolerance of tablets. 200mg in weight the tablet batches have therefore passed the weight variation testing in accordance with IP restrictions. Friability was discovered to be less than 1% Tablet batches pass the friability test as a result . the hardness was determined to be between 3.4 and 3.8 similar of tablet sold.

Table no.3 Evaluation of mixed blend of drug and excipients

Parameter	F1	F2	F3	F4	F5	F6	F7	F8	F9
Angle of repose	28.4 ±1.2	28.7 ±1.1	31.80 ±0.8	31.36 ±1.1	28.78 ±0.8	28.4 ±0.3	30.80 ±0.4	28.4 ±0.7	28.9 ±0.3
Bulk density(gm/cc)	0.878 ±0.023	0.892 ±0.004	0.890 ±0.04	0.883 ±0.012	0.878 ±0.023	0.921 ±0.02	0.95 ±0.026	0.884 ±0.032	0.890 ±0.042
Tapped density(gm/cc)	1.078 ±0.02	1.115 ±0.02	1.105 ±0.003	1.086 ±0.01	1.078 ±0.02	1.053 ±0.03	1.129 ±0.03	1.063 ±0.002	1.085 ±0.02
Carrs's index(I)	18.63 ±0.7	20 ±0.4	19 ±0.5	18.8 ±0.3	18.63 ±0.5	18.4 ±0.5	17 ±0.3	18.5 ±0.2	18.2 ±0.1

It was shown that a higher superdisintegrant content was associated with a lower wetting time and a higher water absorption ratio in all formulations. F1 through F9 . In the cases of croscarmellose sodium and crosspovidone , disintegration time was negatively correlated with the concentration of superdisintegrants;however in the case of sodium starch glycolate , a the formulation F8 has demonstrated favorable outcomes in in terms drug release of 99.78% in 60 minute disintegration time,wetting time ,and water absorption ratio minutes.in terms of disintegration times, least amount of wetting time and water content, formulation F4 has performed better 98%.medication release and absorption ratio and under three minutes. Excellent result has been observed in the water absorption ratio formulation F9.The F9 shows to be least amount the disintegration and wetting time with the medication release 99.38%in just three minutes it was so determined that F8 batch.with content 8% crosspovidone was an optimal batch.

Table no.4 Evaluation of Olmesartan medoxomil Mouth dissolving tablet

Parameter	F1	F2	F3	F4	F5	F6	F7	F8	F9
Hardness kg/cm²	3.6± 0.3	3.7± 0.3	3.6± 0.2	3.8± 0.3	3.4± 0.3	3.7± 0.3	3.4± 0.3	3.8± 0.2	3.8± 0.1
Thickness (mm)	2.41± 0.03	2.40± 0.01	2.38± 0.02	2.28± 0.04	2.36± 0.02	2.38± 0.02	2.35± 0.03	2.48± 0.02	2.31± 0.02
Diameter (mm)	8.0± 0.02	8.08± 0.02	8.07± 0.03	8.13± 0.13	8.10± 0.01	8.13± 0.03	8.20± 0.02	8.20± 0.02	8.10± 0.02
Friablity %	0.89± 0.02	0.88± 0.01	0.81± 0.03	0.68± 0.04	0.79± 0.03	0.85± 0.03	0.88± 0.03	0.78± 0.05	0.54± 0.02
Weight variation	1.3± 0.5	3.5± 0.6	3.6±0.3	2.3± 0.8	2.6± 0.7	2.9± 0.4	3.6± 0.5	3.3±0.4	3.2±0.6
Disintegration time (sec)	33±2	30±1	29±1	30±2	31±3	40±2	40±2	38±3	27±0.3
Wetting time(sec)	37±2	35±2	36±1	38±1	37±2	39±1	32±1	38±1	29±1
Water absorption ratio %	61± 1.32	69.66± 0.9	86.66± 2.6	57.89± 3.3	58± 3.3	60.18± 2.3	71±0.7	80± 1.3	87.22± 2.2
Assay %	96.08± 1.35	105± 2.32	100± 2.1	99.16± 1.5	97.50± 2.3	102.3± 1.6	105.83± 2.6	105.83± 2.4	102.25± 1.8

Table no.5 In vitro dissolution study

Sr.no	Time (min)			% drug release	Formulation					
		F1	F2	F3	F4	F5	F6	F7	F8	F9
1	2	11.22	6.59	17.29	42.63	23.50	21.83	35.93	55.07	40.12
2	5	25.01	13.07	27.90	64.25	38.51	30.68	51.04	61.70	61.50
3	10	32.70	20.80	42.73	70.46	49.42	44.07	64.25	71.20	68.30
4	15	40.05	27.28	53.64	73.62	54.06	49.83	79.59	88.90	71.80
5	20	43.24	32.84	70.02	75.27	56.73	50.87	82.58	90.80	73.60
6	30	49.94	37.70	78.40	75.68	57.13	56.12	86.49	89.69	76.20
7	40	53.64	39.85	82.40	80.82	59.78	57.56	88.55	91.25	81.36
8	50	55.40	42.42	85.77	85.98	68.89	67.55	89.02	97.45	84.64
9	60	65.56	62.91	92.88	91.64	76.81	89.80	91.75	99.80	90.80

VI. CONCLUSION:

The mouth dissolving tablet of the hypertension medication Olmesartan medoxomil was developed in the current study with the goal of enhancing patient compliance and achieving a quick on set of action in the formulation three distinct superdisintegrants – cross-polyvidone sodium starch glycolate and croscarmellose -were employed for a disintegration duration of 27 seconds ,formulation F8 % cross povidone has demonstrated the greatest performance. Compare with the commercial mouth dissolving tablet , the disintegration time is shorter . in the final 3 minutes of the in vitro dissolution testing, 98.38% of the mediation was released .the F8 formulation produce an outstanding overall performance . Formulation F8 was therefore determined to be optimised formulation . olmesartan mouth dissolving pills can thus be produced with good patient compliance.

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