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DEVELOPMENT AND OPTIMIZATION OF ORODISPERSIBLE TABLETS OF SEROTONIN HYDROCHLORIDE

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Keywords:

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ABSTRACT: The aim of the present work is to develop the formulation the orodispersible tablets of Serotonin Hydrochloride. The tablets were prepared by direct compression technique using microcrystalline cellulose (MCC) as directly compressible diluents. Superdisintegrants such as Croscarmellulose sodium (CCS) Sodium starch glycolate (SSG) and Crospovidone were used. **Method:** Using different concentrations of superdisintegrants seven formulations were made and further investigated. The prepared powder mixtures were subjected to both preformulation and physical evaluation studies, and further post compression evaluation parameters including tablet hardness, friability, disintegration time and *in vitro* drug release. **Results:** The pre-compression studies revealed that all formulations were found to be of good flowability. Tablet hardness and friability revealed good mechanical strength. **Conclusion:** After evaluating all the formulations it has been revealed that the tablets exhibited acceptable properties. According to the present study, it was found that tablets of batch F4 (blend containing CCS & crospovidone (15mg) showed better disintegrating property as well as % drug release (98.78% within 40 min).

INTRODUCTION: Orodispersible tablets have received ever-increasing demand throughout the last decade and therefore the field has become a quickly growing area within the pharmaceutical industry [1]. Recent advances in novel drug delivery (NDDS) aims to boost safety and efficaciousness of drug molecule by formulating a convenient dosage form for easy administration and to attain higher patient compliance [2]. Orodispersible tablets are uncoated or film - coated tablets meant to be distributed in water before administration giving a homogenous dispersion.

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The right selection of disintegrates and its consistency of performance are of crucial importance to the formulation development of such tablets. Orodispersible tablets are well administered for the pediatric, dysphasic patients, unstable, uncooperative and ill patients, those with conditions of nausea, sudden episodes of allergic attack or coughing [3]. The basic approaches to develop dispersible tablet include maximising the porous structure of the tablet matrix, incorporating the suitable disintegrating agent and using extremely water soluble excipients in the formulation [4].

Serotonin Hydrochlorine is a monoamine that is biochemically derived from tryptophane and created in serotonergic neurons within the central nervous system and in enterochromaffin cells within the digestive tract [5]. 5-hydroxytryptamine is very important for regulation of mood, sleep,

vomiting, sexuality, and appetency. Low levels of 5-hydroxytryptamine are related to many disorders, as well as depression, migraines, manic-depressive psychosis, and anxiety. Its actions are terminated primarily via uptake of 5-hydroxytryptamine from the junction. Monoamine neurotransmitter uptake may be suppressed with methylenedioxy-methamphetamine, cocaine, tricyclic antidepressant antidepressants, and selective 5-hydroxytryptamine re-uptake inhibitors [6].

MATERIALS AND METHODS:

Preparation of Serotonin Hydrochloride Orodispersible tablets: [7 – 9] All the ingredients were weighed as specified in the formula **Table 1**. Drug diluents, lubricant and disintegrants were passed through sieve # 80. The drug was first mixed homogeneously with diluents and disintegrant in a mortar and pestle and required degree of fineness was attained. Finally magnesium stearate were added and mixed. Different formulations (F1 to F7) were prepared by direct compression technique. The resultant blends after micromeritic evaluations were directly compressed using 8 mm flat punches with tablet weight 220 mg in a single punch rotatory machine. A batch size of 20 tablets was prepared in each formulation.

TABLE 1: FORMULATION OF SEROTONIN HYDROCHLORIDE TABLETS CONTAINING DIFFERENT CONCENTRATION OF SUPERDISINTEGRANTS

Ingredients(mg)	F1	F2	F3	F4	F5	F6	F7
Serotonin Hydrochloride	150	150	150	150	150	150	150
MCC	25	25	25	25	25	25	25
Vanillin	10	10	10	10	10	10	10
Talc	2	2	2	2	2	2	2
Magnesium stearate	5	5	5	5	5	5	5
Croscarmellulose sodium	30	-	-	15	-	15	10
Crospovidone	-	30	-	15	15	-	10
Sodium starch glycolate	-	-	30	-	15	15	10

Precompression Evaluation of Powder Blend:

Angle of Repose (θ): The frictional force in a loose powder can be measured by angle of repose. Angle of repose is defined as the maximum angle possible between the surface of a pile of the powder and horizontal plane. It is determined by using fixed funnel method. The granules were poured through a funnel that can be raised vertically until a maximum cone height was obtained. The radius of the heap was measured, as angle of repose was calculated by using formula: [10-12]

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

Where, θ = Angle of repose
h = Height of pile
r = Radius of the base of pile

Bulk density (Db): It is the ratio of total mass of powder to the bulk volume of powder. Bulk density was determined by pouring the powder into graduated cylinder. The bulk volume and mass of the powder was noted. It is expressed in gm/cc and bulk density was calculated by using formula:

$$Db = M/Vb$$

Where, M = Mass of powder
Vb = Bulk volume of the powder

Tapped density (DT): It is the ratio of total mass of powder to the tapped volume of powder. The measuring cylinder containing known mass of powder tapped for a fixed time. The maximum volume occupied in the cylinder and weight of the granules was measured. It is expressed in gm/cc, tapped density can be calculated by using formula:

$$Dt = M/Vt$$

Where, Dt = Tapped density
M = Mass of powder
Vt = Tapped volume of the powder

Carr's Consolidation Index: Specific amount of powder was transferred to measuring cylinder and the initial volume occupied was noted as (Vb) and the content was tapped for 100 times and the volume was noted (Vt). Then calculated the Carr's consolidation index by using the following formula:

$$\text{Carr's consolidation index} = (Vt\text{-}Vb/Vt) \times 100$$

Where, Vb = Bulk volume
Vt = Tapped volume

Hausner's Ratio: Hausner's ratio is an indirect index of ease of powder flow.

Hausner's ratio can be determined by the following equation:

Hausner's ratio = TBD / LBD

Where, TBD = Tapped bulk densities
LBD = Loose bulk densities

TABLE 2: PRECOMPRESSION EVALUATION OF DISPERSIBLE TABLET BLEND OF SEROTONIN HYDROCHLORIDE MEAN ± SD N=3

S. no.	Formulation	Angle of Repose (θ)	Bulk Density(g/cc)	Tapped Density(g/cc)	Carr's index	Hausner's ratio
1	F1	28.45±1.46	0.43±0.01	0.52±0.012	16.22±0.43	1.30±0.010
2	F2	30.58±1.47	0.42±0.02	0.51±0.016	16.84±0.60	1.31±0.034
3	F3	28.95±1.31	0.44±0.03	0.55±0.012	17.16±0.37	1.31±0.011
4	F4	29.61±1.23	0.45±0.01	0.55±0.012	16.46±1.25	1.32±0.030
5	F5	29.28±0.85	0.45±0.00	0.55±0.016	16.72±0.75	1.33±0.034
6	F6	30.86±1.44	0.43±0.00	0.52±0.021	17.22±0.51	1.31±0.032
7	F7	29.17±0.98	0.44±0.30	0.55±0.026	16.43±1.12	1.31±0.028

Post Compression Evaluation of Tablets: [13 - 18]

Dispersibility Test: [13] Two tablets were placed in 100 ml of distilled water and stirred until completely dispersed. A smooth dispersion is produced, which passes through a sieve screen with a nominal mesh aperture of ASTM#22.

Disintegration Test: [13 - 14] One tablet was kept in each tube of the disintegration apparatus, suspended the assembly in the basket containing water and operated with the discs for 4 minutes, unless otherwise stated in the individual monograph. Remove the assembly from the liquid. Dispersible tablet should complete the disintegration within 3 minutes in water temperature 15 ºC to 25 ºC.

% Drug Content Uniformity: Twenty tablets were powdered, and 150 mg equivalent weight of Serotonin Hydrochloride in powder was accurately weighed and transferred into a 100 ml volumetric flask. Initially, 50ml of acidic buffer (pH 1.2) was added and shaken for 10 min. Then, the volume was made up to 100 ml with phosphate buffer. The solution in the volumetric flask was filtered, diluted suitably and analyzed spectrophotometrically at 345 nm. The drug content in each tablet was calculated using the standard calibration curve of Serotonin Hydrochloride in pH 1.2.

***In-vitro* Dissolution Studies:** Dissolution studies for all the formulated tablets were carried out using USP paddle method at 75rpm in 900 ml of 0.1 N HCl at 37 ºC as dissolution media. 5 ml aliquot was withdrawn at the specified time intervals and assayed spectrophotometrically at 345 nm. An equal volume of fresh medium, which was prewarmed, was replaced into the dissolution media after each sampling to maintain the constant volume throughout the test.

Thickness, Hardness, Friability and Weight Variation Studies: Tablets from all the seven formulations were evaluated for its various properties like thickness diameter using digital vernier calipers, hardness by using Monsanto hardness tester, friability by using roche friabilator and weight variation by using a electronic balance.

TABLE 3: POST-COMPRESSION EVALUATION OF ORODISPERSIBLE TABLET OF SEROTONIN HYDROCHLORINE

S. no.	Formulation	Hardness* (kg/cm^2)	Thickness* (mm)	Friability# (%)	**Weight variation	**Drug Content
1	F1	5.75±0.27	4.26±0.12	0.600	0.219±0.0038	82.19±0.7
2	F2	6.00±0.31	4.25±0.10	0.632	0.220±0.0020	85.9±0.8
3	F3	5.91±0.20	4.18±0.07	0.613	0.221±0.0022	49.62±0.4
4	F4	6.00±0.31	4.23±0.08	0.650	0.218±0.0021	91.23±0.3
5	F5	6.08±0.37	4.11±0.11	0.525	0.220±0.0021	82.23±0.1
6	F6	6.00±0.31	4.26±0.12	0.587	0.221±0.0023	86.23±0.6
7	F7	5.80±0.31	4.20±0.10	0.687	0.217±0.0023	89.36±0.9

Mean ±SD *n=6, **n=10 and #n=10

RESULTS AND DISCUSSION:

Characterization of Amoxicillin Trihydrate Dispersible Powder Blend: The formulation showed good flow property and compressibility index. Angle of repose ranged from 28º.451-30º.861, Carr's index ranged from [16 - 17]. The LBD

and TBD of the prepared granules ranged from 0.42 - 0.45 and 0.51 - 0.55 g/cc respectively, Hausner's ratio was found to be 1.30 - 1.33. The results of angle of repose indicates good flow property of the granules and the value of Carr's index further showed support for the flow property. The result were showed in **Table 2**.

Characterization of Serotonin Hydrochlorine Dispersible Tablet: The tablets with weight of 220mg subjected to quality control tests such as weight variation, Hardness, Friability and Thickness **Table 3**. All formulation products lied within the pharmacopoeial requirement within ±7.5 for weight variation. The mean values for hardness was within 5.75 - 6.08 kg/cm^2 and all formulations exhibits friability within the 0.52- 0.68% during the friability determination. The thickness was found in the range of 4.11 - 4.26 mm. The results showed good mechanical strength and had uniformity size of the tablets.

Disintegration Test and Dispersibility Test: Disintegration is the most important characteristic test of dispersible tablet, among the formulation (F4) formulated with croscarmellulose sodium and crospovidone shows excellent disintegration time of 38 sec. All the formulation passed the dispersibility test.

***In-vitro* Dissolution Study:** In formulation F1, F2, F3 were formulated with single superdisintegrants, Croscarmellulose sodium, Crospovidone, Sodium starch glycolate and respectively were used along with the drug, the release of the drug from the F1 and F2 was showed satisfactory result. F3 shows better drug release from the formulation. F4 were formulated with crospovidone and croscarmellulose sodium shows an excellent release of the drug from the formulation. F5 formulated with crospovidone and sodium starch glycolate shows increased drug release.F6 with sodium starch glycolate and croscarmellulose sodium with good release of the drug. The F7 formulated with crospovidone, croscarmellulose sodium and sodium starch glycolate showed satisfactory drug release due to combination of three superdisintegrant agent with low ratio. When comparing to the above formulation, F4 showed excellent drug release. It was considered as an optimized formulation in this work.

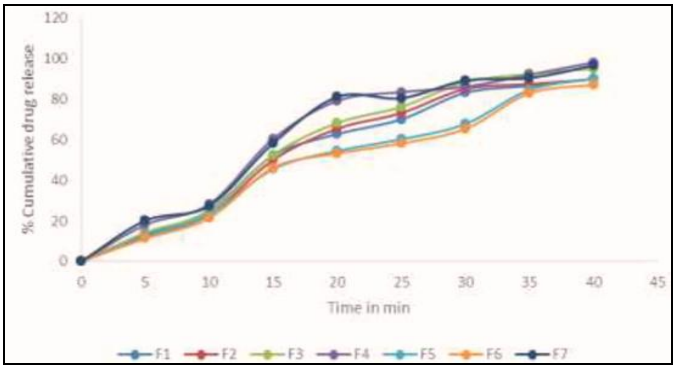

FIG. 1: *IN-VITRO* DISSOLUTION STUDY

CONCLUSION: The present study shows that Serotonin Hydrochlorine Orodispersible tablet dosage form formulated by direct compression technique. The *in-vitro* study shows formulation F4 is well suited to orodispersible tablet formulation due to the disintegration time of just 38 sec, which is formulated by using superdisintegrents croscarmellulose and crospovidone.

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CONFLICT OF INTEREST: The authors declare that there are no conflicts of interest.

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