FORMULATION AND EVALUATION OF MOUTH DISSOLVING TABLET OF SESBANIA GRANDIFLORA EXTRACT USING NOBLE CO-PROCESS TECHNIQUE

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ABSTRACT

The powdered leaves and flower of *Sesbania grandiflora* extracted with different solvent. The resultant extract was dried in air until constant weight of the plant extract was obtained. The plant extract was then observed for the physical characteristics. Physically *S. grandiflora* plant extracts was blackish green in color, bitter in taste and sticky in nature. The solubility analysis of leaves and flower extract of *S. grandiflora* was performed by using different solvents of variable polarity. The plant extract showed good solubility in variable solvents. The extracted value of *S. grandiflor*a was found to be 15.4. Co-processed superdisintegrants were prepared by solvent evaporation using crospovidone and croscarmellose sodium in different ratios (1:1, 1:2. & 1:3). The co-processed superdisintegrants were evaluated for their flow and compression properties in comparison with physical mixture of superdisintegrants. The angle of repose of co-processed superdisintegrants was found to be <25o which indicate excellent flow in comparison to physical mixture of superdisintegrants (>30o) due to granule formation, Carr's index in the range of 10-15% and Hausner's ratio in the range of 1.10-1.14. In vitro disintegration studies on the promising formulation CPF5, control (CFF1) and commercial conventional formulations (CCF) were carried out in pH 6.8 phosphate buffer. From the evaluation parameters, it was observed that 4% co-processed superdisintegrant (1:1 mixture of crospovidone and feugreek seed mucilage) was the optimum concentration for rapid tablet disintegration on the basis of the least disintegration time observed with CPF5 formulation. The superdisintegrant action of Sodium Starch Glycolate resulted in hydrophilicity and swelling which in turn causes rapid disintegration.

KEYWORDS: Mouth Dissolving Tablet, bioavailability, herbal, Co-Processing, Superdisintegrant

INTRODUCTION

The development of an appropriate dosage form for older people, children, bed ridden patients, mentally retarded, uncooperative, nauseated patients been widely desired as it become difficult for these patients to swallow conventional. tablets **(Kremzar L. et al, 1998)** Co-processing is based on the novel concept of two or more excipients interacting at the sub particle level, the objective of which is to provide a synergy of functionality improvement as well as masking the undesirable properties of individual.**(Gohel MC et al,2007)** Co-processing excipients leads to the formulation of excipient granules with superior properties compared with physical mixtures of components or individual components5. The concept of formulating fast dissolving tablets (FDT) of metoclopramide hydrochloride (anti-emetic) using co-processed superdisintegrants which increase the water uptake with shortest wetting time and thereby decrease the disintegration time of the tablets by simple and cost effective (at low concentration of superdisintegrants) direct compression technique. **(Fu, Y et al,2004)**

Tablets designed to dissolve on the buccal (cheek) mucous membrane were a precursor to the Mouth Dissolving Tablet (MDT). Absorption through the cheek allows the drug to bypass the digestive tract for rapid systemic distribution. A fast disintegration time and a small tablet weight both can enhance absorption in the buccal area. **(Wehling Fred et al, 1993).** The first MDTs disintegrated through effervescence rather than dissolution, and were designed to make taking vitamins more pleasant for children. Dissolution became more effective than effervescence through improved manufacturing processes and incorporation of ingredients (such as the addition of mannitol which increase the binding and decrease dissolution time **(Blank et al, 1990; Kuchekar et al 2004).** Increase the bioavailability of the drug and rapid absorption through pregastric absorption of drugs from mouth, pharynx and

oesophagus as saliva passes down. **(Shishu.,et al2003).** Good mouth feel property of true mouth dissolving tablets helps to change the perception of medication as "bitter pill" **(Brown, 2003)** No risk of suffocation in airways due to physical obstruction when swallowed, thus providing improved safety and compliance.

MATERIALS AND METHODS

Procurement of excipients: The drug, excipients, chemicals/ reagents and equipments used for various experiments are Fenugreek seed mucilage (FSM) and Crospovidone were purchased from Yarrow chemicals Mumbai, Maharashtra and are of AR grade.

Collection of plant material: The plant Sesbania grandiflora was collected from Medicinal garden of UIPS, Ujjain, M.P. and was authenticated by Dr. S. N. Dwivedi, Prof. & Head, Department of Botany, Janata PG College, APS, University, Rewa, M.P. and Voucher specimen No. SD/SG/2120 was deposited in our department.

Preparation of plant powder: The plant was dried under shade and then powdered coarsely with a mechanical grinder. The powder was passed through sieve No. 40 and stored in an airtight container for further use.

Preparation of extracts: About 250 g of dried powder leaf of plant was subjected to Soxhlet apparatus. It was fist defatted with petroleum ether then exhaustively extracted with ethyl acetate solvent in a Soxhlet apparatus for 36 hours. The temperature was maintained at (40-50oC). The solvents were removed by distillation under reduced pressure and the resulting semisolid mass was vacuum dried using rotary flash evaporator to obtain the extract.

Determination of Extractive value: The extractive values of dried leaf and bark powder of *Sesbania grandiflora* were determined by formula as mentioned below:

% Extractive yield (w/w) = weight of dried extract / weight of dried fruit × 100

Preparation of Co-processed Superdisintegrants

The co-processed superdisintegrants were prepared by solvent evaporation method. A blend of crospovidone and fenugreek seed mucilage (in the ratio of 1:1, 1:2 & 1:3) was added to 10 ml of ethanol. The contents of the beaker (250 ml capacity) were mixed thoroughly and stirring was continued till most of ethanol evaporated. The wet coherent mass was granulated through # 44-mesh sieve. The wet granules were dried in a hot air oven at 60º C for 20 minutes. The dried granules were sifted through # 44-mesh sieve and stored in airtight container till further use. **(Fu, Y et al,2004)**

Pre-compression Studies: Various formulations and process variables were involved in mixing of ingredients and all these can affect the properties of the blends produced. Various evaluation parameters of blends tested Bulk density, Tapped Density, Compressibility Index, Hausner ratio, Angle of repose,

Preparation of fast dissolving tablets by direct compression method:

Fast dissolving tablets of *Sesbania grandiflora* extract were prepared by direct compression. All the ingredients (except granular directly compressible excipients) were passed through # 60-mesh separately. Then the ingredients were weighed and mixed in geometrical order. Powder blend was evaluated for bulk density, tapped density, Carr's index and Hauser's ratio.Compressed into tablets of 350mg using 8mm round flat punches on 10-station rotary tablet machine (Clit).(**Gohel MC et al,2007)**

Table No. : Formula for different batches of Terbutaline Sulphate tablets

Ingredients	CF F1	PM F2	PM F3	PM F4	CP F5	CP F6	CP F7
Sesbania grandiflora extract	250	250	250	250	250	250	250
Mannitol	55	55	55	55	55	55	55
Sodium Saccharin	10	10	10	10	10	10	10
Superdisintegrants (CP+FSM)	-	15	15	15	15	15	15
Aerosil	16	16	16	16	16	16	16
Pre-gelatinised Starch	1.5	1.5	1.5	1.5	1.5	1.5	1.5

Menthol	1.5	1.5	1.5	1.5	1.5	1.5	1.5
Magnesium stearate	1.0	1.0	1.0	1.0	1.0	1.0	1.0

Evaluation of Fornmulated fast dissolving Tablet

Hardness:. 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 . Hardness of tablet was evaluated by Monsanto hardness tester or Pfizer tester. Hardness was measured in kg/cm2 and for tablet it is above 4-6 kg/cm^2.

Friability: This test is applicable to compressed tablets and is intended to determine the physical strength of tablets. It was evaluated by Roche Friabilator with 100 revolution rotating 25 per minute for 4 min by using 6 tablets. According to USP tablet should have limit < 1%. for acceptance. Following formula was used to calculate the friability.

%F=1- (loss in weight/initial weight)100

Weight variation: Weight variation was calculated as per method describe in USP.20 tablets was weighed individually and the average wias calculated.The requirements are met if theweight of not more than 2 of tablets differ by more than percentage listed in the tablet and no tablets differ by in weight by more than double that percentage.

Table No.7.2: Percentage weight variation of tablet (IP)

S. No	Average weight of individual tablet	Limits (%)
1	< 130	10
2	130-324	7.5
3	> 324	5

Wetting Time and Water Absorption Ratio (R): Twice folded tissue paper was placed in a petri dish having an internal diameter of 5 cm containing 6 ml of water. A tablet was carefully placed on the surface of the tissue paper in the Petri dish. The time required for water to reach the upper surface of the tablet and to completely wet it was noted as the wetting time. Water absorption ratio (R) was then determined according to the following equation:

R= 100x(Wa-Wb)/Wb

Where; Wb and Wa were tablet weights before and after water absorption, respectively.

Disintegration test: Disintegration test was measured using disintegration test apparatus. The test was carried out on 6 tablets using Digital Tablet Disintegration Tester. Distilled water at 37°C ± 2°C was used as a disintegration media. One tablet was placed in each of the six tubes of disintegration test apparatus. I.P. method was followed without using disc. The time required for complete disintegration of tablet with no palatable mass remaining in each tube was determined using stop watch.

Thickness variation: Ten tablets from each formulation were taken randomly and their thickness was measured with a micrometer screw gauge.

RESULTS AND DISCUSSION

Physical characteristics of *S. grandiflora* plant extracts were blackish green in color characteristic odor bitter and bit sticky. The solubility analysis of leaves and flower extract of *S. grandiflora* was performed by using different solvents of variable polarity. The plant extract showed good solubility in variable solvents.

Extractive Value: The extracted value of *S. grandiflora* was found to be 15.4

Table No. : Data of Solubility Determination of Terbutaline Sulfate

S. No.	Name of solvents	Solubility at 25° C
1	Water	Slightly soluble

2	Methanol	Completely soluble
3	Ethanol	Completely soluble
4	Benzene	Completely soluble
5	Chloroform	Slightly soluble
6	Diethyl	Slightly soluble

Pre-compression Studies of Co-processed superdisintegrants

Co-processed superdisintegrants were prepared by solvent evaporation using crospovidone and croscarmellose sodium in different ratios (1:1, 1:2. & 1:3). The co-processed superdisintegrants were evaluated for their flow and compression properties in comparison with physical mixture of superdisintegrants. The angle of repose of co-processed superdisintegrants was found to be <25o which indicate excellent flow in comparison to physical mixture of superdisintegrants (>30o) due to granule formation, Carr's index in the range of 10-15% and Hausner's ratio in the range of 1.10-1.14.

Table No. : Pre-compression Parameters of Co-processed Superdisintegrants and Physical Mixture of Superdisintegrants

Parameters	Formulation Code					
	PM1	**PM2**	**PM3**	**CP1**	**CP2**	**CP3**
Bulk density (g/cc)	0.37	0.36	0.42	0.23	0.26	0.29
Tapped density (g/cc)	0.46	0.42	0.49	0.26	0.26	0.31
Angle of repose (degree)	31	30	36	24	25	25
Carr's index (percent)	14	15	13	12	12	12
Hausner's Ratio	1.14	1.13	1.14	1.14	1.12	1.12

Table No. : Pre-compression Parameters of *S. grandiflora* FDT Formulations Prepared by Direct Compression Method

Parameters	Formulation Code						
	CPF1	**PMF2**	**PMF3**	**PMF4**	**CPF5**	**CPF6**	**CPF7**
Bulk density (g/cc)	0.55	0.53	0.53	0.54	0.51	0.53	0.53
Tapped density (g/cc)	0.62	0.60	0.62	0.63	0.58	0.59	0.58
Angle of repose (degree)	30.27	29.21	30.2	29.35	27.93	29.02	28.57
Carr's index (percent)	16	13	12.55	12.65	12.3	11.58	13.2
Hausner's Ratio	1.08	1.14	1.12	1.13	1.13	1.12	1.13

Evaluation of Formulated fast dissolving Tablet

Fast dissolving tablets of *S. grandiflora* extract were prepared using co-processed superdisintegrants and physical mixture of superdisintegrants. Directly compressible mannitol (Pearlitol SD 200) was used as a diluents to enhance mouth feel. A total of six formulations and control formulation CP0 (without superdisintegrant) were designed. As the blends were free flowing (angle of repose <300 and Carr's index <15%), tablets obtained were of uniform weight (due to uniform die fill), with acceptable variation as per IP specification i.e., below 5%.. Hardness of the tablets was found to be in the range of 2.96-3.13 kg/cm2. Friability below 1% was an indication of good mechanical resistance of the tablets. Water absorption ratio and wetting time, which are important criteria for understanding the capacity of disintegrants to swell in presence of little amount of water were found to be in the range of 44-85% and 30-106 sec respectively. Among all the designed formulations, formulation, CPF5 was found to be promising and displayed an in vitro dispersion time of 30 sec, which facilitates their faster dispersion in the mouth.

Overall, the formulation CPF5 containing 4% w/w of co-processed superdisintegrant (1:1 mixture of crospovidone and feugreek seed mucilage) was found to be promising and has shown an in vitro dispersion time of 30 sec, wetting time of 34 sec and water absorption ratio of 85% when compared to the formulation PMF2 containing 4% w/w of Physical mixture of superdisintegrant (1:1 mixture of crospovidone and feugreek seed mucilage) which shows 36sec, 38 sec, 75% and control formulation (CPF1) which shows 98 sec, 104 sec and 45% values respectively for the above parameters.

***In-Vitro* Disintegration Test:**

In-vitro disintegration studies on the promising formulation CPF5, control (CFF1) and commercial conventional formulations (CCF) were carried out in pH 6.8 phosphate buffer. From the evaluation parameters, it was observed that 4% co-processed superdisintegrant (1:1 mixture of crospovidone and feugreek seed mucilage) was the optimum concentration for rapid tablet disintegration on the basis of the least disintegration time observed with CPF5 formulation. The superdisintegrant action of Sodium Starch Glycolate resulted in hydrophilicity and swelling which in turn causes rapid disintegration.

Table No.: Evaluation of Terbutaline Sulphate FDT Formulations

Parameters	CP0	PM F2	PM F3	PM F4	CP F5	CP F6	CP F7
Hardness(kg/cm^2* ± SD	2.86 ± 0.05	2.88 ± 0.1	2.82 ± 1.4	3.25 ± 0.05	3.12 ± 0.04	3.22 ±0.05	3.23 ± 0.03
Thickness* (mm)	2.17 ± 0.02	2.23 ± 0.02	2.23 ± 0.05	2.75.0 ± 0.01	2.21 ± 0.02	2.23 ±0.01	2.22 ± 0.01
In-vitro Dispersion time (s)* ± SD	98 ± 2	36.31 ± 1.52	40.23 ± 0.77	42.33 ± 2.52	30 ± 2	36.33 ±3.41	39.45 ± 2.0
Wetting time (s)* ± SDs	104 ± 4.93	37.86 ± 1.52	42.23 ± 1	45.313 ± 1.5	33.67 ± 0.5	36.83 ±1.52	40.96 ± 1.15
Water Absorption ratio (%)* ± SD	45 ± 1	75.33 ± 1.15	72.66 ± 1.52	64.23 ± 1	85.46 ± 1	77.0 ±2.08	703.14
Weight Variation (%)	345-358 mg (IP limits ± 5%)						

CONCLUSION

Summary In the present research work an attempt has been made to optimize, formulate and characterize fast dissolving tablet (s) of. Co-processed superdisitegrants consisting of crospovidone and feugreek seed mucilage *Sesbania grandiflora* exhibited good flow and compression characteristics. *Sesbania grandiflora* tablets containing co-processed superdisintegrants exhibited quick disintegration and improved drug dissolution. This formulation is more cost effective than aerosol inhalation pumps available. The tablets disintegrated within 50 sec under experimental in vitro laboratory conditions. It can be concluded from the present work that co-processed superdisintegrants of crospovidone and feugreek seed mucilage are superior to physical mixture of crospovidone and croscarmellose used in herbal plant extract *Sesbania grandiflora* fast dissolving tablets.

CONFLICTS OF INTEREST

There are no conflicts of interests.

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