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PEANUT HUSK POWDER AS A SUPER-DISINTEGRATING AGENT IN THE FORMULATION OF FAST DISSOLVING TABLETS OF DOMPERIDONE

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ABSTRACT

The rapid growth of novel drug delivery systems has resulted in an increase in the number of excipients being used in solid dosage forms in pharmaceutical industry. This includes both new materials and new physical forms of existing materials to improve the physicochemical properties of tablet dosage forms. The aim of the present work was to evaluate peanut husk powder, as a disintegrating agent in the formulation of fast dissolving tablets of Domperidone. Total six formulations were designed using different disintegrating agents and quality control tests like weight variation, hardness, friability, disintegration and dissolution were carried out for the prepared tablets. The obtained results were tabulated and analyzed. The prepared tablets were found to pass all the quality control tests performed. The formulation containing peanut husk powder as disintegrating agent was found to be the best formulation among all others. Peanut husk powder obtained from natural plant seeds was found to be a promising super-disintegrating agent from this research work.

KEYWORDS: Fast dissolving tablets, peanut husk powder, super-disintegrating agent, Domperidone, swelling capacity, wetting time.

INTRODUCTION

Fast dissolving tablets also known as fast melt or fast disintegrating tablets rapidly dissolve or disintegrate into a fine dispersion in the mouth without the need for any more drinking water. These dosage forms are regarded as a part of novel drug delivery systems. The main advantage of these dosage forms involves the combination of the benefits of solid and liquid formulations of oral route of administration. They offer practical solution for pediatric and geriatric patients, who experience difficulty in swallowing also called as dysphasia.[1] They also increase the bioavailability of poorly water soluble drugs by enhancing the dissolution profile of the drug.[2] The formulation of the old drug substances into new dosage forms allows pharmaceutical companies to extend the patent life and market exclusivity. Thus pharmaceutical industry has both scientific as well as commercial reasons for investing in this relatively new technology. Remarkable scientific literature was also reported from different laboratories in this area of research.[3-5]

Disintegrating agents play crucial role in the formulation of fast dissolving tablets. Natural materials are easily and economically available and form a vital source for further development as pharmaceutical excipients. Murali Mohan Babu G.V., *et al* developed modified Gum karaya and it showed excellent disintegrating property when compared to Gum karaya[6]. *Plantago ovata* mucilage and husk powder and *Ocimum basillicum* mucilage and seed powder were also reported as disintegrating agents in the formulation of Ibuprofen dispersible tablets.[7] Gattani S.G., *et al* prepared treated agar powder and studied its disintegrating agent properties. Treated agar powder was found to be more effective disintegrating agent than agar powder in their studies.[8] Diltiazem Hydrochloride dispersible tablets were formulated employing varying concentrations of mucilage isolated from the plant *Linum usitatissimum* (Linseed) and the study has revealed the effectiveness of linseed mucilage powder as a disintegrating agent.[9] Based on the literature survey, as a part of natural material excipients concept, it was planned to evaluate peanut husk powder as a disintegrating agent. The present research work was aimed at studying the peanut husk powder as disintegrating agent in the formulation of fast dissolving tablets of Domperidone. Domperidone is a dopamine receptor antagonist with antinauseant and prokinetic effects.[10] The systemic bioavailability of Domperodone is only about 15% in fasting subjects given a dose by mouth, although this is increased when Domperidone is given after food. The low bioavailability is thought to be due to first-pass hepatic and intestinal metabolism. It has a terminal elimination half-life of about 7.5 hours.[11] Formulation of fast dissolving tablets of Domperidone might improve its dissolution rate and bioavailability.

MATERIALS AND METHODS

Domperidone was obtained as a gift sample from Dr. Reddy's laboratories, Hyderabad. Potato starch, pregelatinised starch, croscarmellose, sodium starch glycolate, crospovidone and microcrystalline cellulose were procured from Yarrow chem products, Mumbai. Lactose (Loba chemie), mannitol (Loba chemie), aspartame (S.D. fine chemicals), sodium lauryl sulphate (Fisher scientific), hydrochloric acid (Nice chemicals), talc (Nice chemicals Ltd), magnesium stearate (Qualikems Fine chemicals) were procured commercially. Peanuts were procured from the 'more' super market. All other chemicals were of analytical grade.

Preparation of peanut husk powder

Peanut husk powder (PHP) was prepared from the seeds of *Arachis hypogaea*. Peanut seeds were collected from the super market. The collected seeds were placed in an oven at 50°C for three hours to roast them. The thin, pink outer skin was scrapped from the seeds by manual procedure. The obtained husk was soaked in distilled water overnight, cleaned and dried again. The obtained material was milled into a fine powder utilizing a mixer grinder. The obtained peanut husk powder was passed through sieve no. 80 and the fine powder was stored in a desiccator. It was dried in an oven at 70°C for 2 hours before use.

Surface morphology

The particles of peanut husk powder were mounted on double side carbon tape and coated with a thin gold layer. The surface morphology was analyzed with scanning electron microscope (SEM JEON-JLN 660). The obtained images were utilized for size analysis with the same computer.

Swelling capacity

The swelling capacity of PHP and other disintegrating agents was determined according to the following procedure. 1g of the disintegrating agent was taken in a 50 ml capacity measuring cylinder. 20 ml of distilled water was poured into it. The measuring cylinder was shaken vigorously for 10 minutes and allowed to stand for 24 hours. Swelling capacity was expressed as percentage and calculated using the following equation.[12]

Swelling capacity = $(V_2 - V_1) / V_1 \times 100$

V_2 = Final volume occupied by swollen material after 24 hours

V_1 = Initial volume occupied by the powder in the measuring cylinder

Preparation of tablets

Domperidone, lactose, microcrystalline cellulose (MCC PH 102) and mannitol were taken in a clean and dry mortar and mixed with disintegrating agent for sufficient time (10 minutes). PHP was thoroughly dried in the oven before use. Sodium lauryl sulphate, talc, magnesium stearate and aspartame were added to the mortar and continued mixing for some more minutes. The pre-compression studies were performed for the powder blend. Tablets were compressed by direct compression method using 7 mm standard punches of rotary tablet machine (Shakti, 8-stations). Compression force was kept constant for all the formulations. Disintegrating agents were used at 5% concentration and the quantities of all other ingredients were shown in Table 2.

MCC and mannitol were used as direct compression materials. Lactose was used as a diluent. Aspartame was used as sweetening agent to mask the bitter taste of the drug. Sodium lauryl sulphate was used as surfactant to improve the wetting of the tablets. Talc and magnesium stearate were used as glidant and lubricant respectively.

EVALUATION OF PRE-COMPRESSION POWDER BLEND

Bulk density and tapped density

Weighed amount of powder was poured into a 20 ml measuring cylinder and initial volume (V_o) was measured. The measuring cylinder was arranged on a bulk density apparatus (Electrolab). The apparatus was operated for 100 tapings and then the final volume (V_f) was measured. Bulk density and tapped density were calculated for the individual disintegrating agents and for different formulations.

$$\text{Bulk density } (D_b) = \frac{\text{Weight of the powder}}{\text{Initial volume } (V_o)}$$

$$\text{Tapped density } (D_t) = \frac{\text{Weight of the powder}}{\text{Final volume } (V_f)}$$

Compressibility index and Hausner ratio

The compressibility index and Hausners ratio are a measure of the propensity of a powder to be compressed. The compressibility index and Hausner ratio were calculated using bulk density (D_b) and tapped density (D_t) as follows.[13]

$$\text{Compressibility index} = \frac{D_t - D_b \times 100}{D_t}$$

$$\text{Hausner ratio} = \frac{D_t}{D_b}$$

Angle of repose

The flow property of the powder blend was evaluated by determining angle of repose. Due to frictional forces between the particles, the flow of powder decreases. These frictional forces are quantified by angle of repose. Angle of repose is defined as the maximum angle possible between the surface of a pile of the powder and the horizontal plane. Angle of repose is calculated by the following equation.

$$\tan \theta = \frac{h}{r}$$

where,

θ = Angle of repose

h = Height of the pile

r = Radius of the base of the pile

EVALUATION OF TABLETS

The prepared tablets were evaluated for weight variation, hardness, friability and drug content. Hardness of tablets was tested using Monsanto hardness tester. Friability of tablets was determined by using friability test apparatus (Sisco). Twenty tablets were weighed and taken in the drum of the apparatus that revolves at 25 rpm and dropping the tablets from a distance of six inches with each revolution. After 4 minutes the tablets were collected, dedusted and weighed again. The percent loss in tablets weight was determined. Weight variation was determined by taking 20 tablets and these tablets were individually weighed using electronic balance (Shimadzu AY 220). The drug content was estimated using UV spectrophotometer (Elico, SL 159) at a λ max of 286 nm with 0.1 N hydrochloric acid as the reagent.

The disintegration time was determined by using disintegration test apparatus (Veego). Six tablets were selected randomly from each formulation. One tablet was placed in each tube of disintegration apparatus and the test was carried out without discs, in distilled water at 37±5°C. The mean and standard deviation of time to disintegrate for six tablets was calculated and reported.

Wetting time and water absorption ratio

A piece of tissue paper folded in double was placed in a petri dish containing 6 ml of distilled water mixed with a few drops of water soluble dye. Then a tablet was placed at the center of the wet tissue paper. The time required for the distilled water to diffuse from the paper throughout the entire tablet surface was recorded using a stop watch. Then wetted tablet was weighed. The water absorption ratio (R) was calculated using the following formula.[14]

$$R = \frac{100 \text{ X } (W_a - W_b)}{W_b}$$

where, W_a = Weight of tablet after absorption

W_b = Weight of tablet before absorption

Dissolution studies

Dissolution study for Domperidone fast dissolving tablets was performed using USP dissolution apparatus (Electrolab, TDT-08L) type I at 50 rpm. The dissolution medium used was 900 ml of 0.1N hydrochloric acid maintained at 37±5 °C. Aliquots of 5ml were withdrawn at particular time intervals and the drug content was estimated by using UV spectrophotometer at a λ max of 286 nm.[15] An equal volume of the fresh medium was replaced into the dissolution basket to maintain constant level of the volume. This study was performed on 3 tablets and the average was calculated.

RESULTS AND DISCUSSION

In India, Peanut (groundnut) is one of the most important oilseed crops. Peanuts are rich protein food source that contain many vitamins, minerals. Peanut oil is edible and used for cooking in kitchen. Peanut skin contains an abundant amount of natural antioxidants and a high amount of dietary fiber.[16] A fine and characteristic flavored, light brown colored powder was obtained by milling the skin of the seeds of the plant *Arachis hypogaea*. In the earlier studies, conducted in our laboratory peanut husk powder was employed as a low density excipient in the formulation of floating matrix tablets of Ramipril.[17] The results presented in Table 1 shows that peanut husk powder has a bulk density and tapped density of 0.293 gm/cc and 0.458 gm/cc respectively and it is found to be a light weight powder when compared with all other disintegrating agents employed in this study whose values are also reported in the same Table.

Swelling capacity is a critical factor to understand the disintegration ability of a disintegrating agent. Peanut husk powder does not show any significant swelling property and pregelatinised starch shows the highest swelling capacity as given in Table 1. The swelling capacity of the various disintegrating agents in the decreasing order is pregelatinised starch > sodium starch glycolate > croscarmellose > potato starch >crospovidone > peanut husk powder. The SEM photos (Fig. 1) shows the smooth and spherical shape of peanut husk powder. The absence of dark shades on the spherical structures also indicates the non-interacting nature of the powder. From the size analysis (Fig. 2) it was found that the peanut husk powder particles are uniform and present in the size range of 1.23 – 7.58 µm.

Six formulations as shown in Table 2 were designed and the tablets were prepared by direct compression method. The pre-compression results of the powder blend evaluation were reported in Table 3. The angle of repose values ranges from 25 to 30 which indicate good flow property. The compressibility index value ranges from 13 to 16 which also indicate good flow property. Hausner ratio values are less than 1.25 which indicated that the powder blend exhibited good flow which is an essential requirement for tablet compression.

The results of evaluation of the prepared tablets were reported in Table 4 as post-compression parameters. The tablets showed sufficient hardness to withstand transportation and handling. The friability values found were less than 1% and hence were well within the limits. The weight variation test results indicated that the variation between weights of different tablets is within the acceptable limits. The obtained drug content results indicate that the tablets contain were not less than 95% and not more than 105% of the stated amount of Domperidone. The disintegration time and wetting behavior of the tablets were reported in Table 5. The formulation containing potato starch showed the highest disintegration time and peanut husk powder showed the least disintegration time. The disintegration time of the prepared tablets in the decreasing order was potato starch > pregelatinised starch > croscarmellose > sodium starch glycolate > crospovidone > peanut husk powder. Although pregelatinised starch showed the highest swelling capacity (Table 1) its disintegration ability was

not at the same order. Wetting time and water absorption ratio of all the formulations were shown in Table 5. Faster wetting was shown by formulation F6 containing peanut husk powder as a disintegrating agent due to capillary action. Maximum water uptake was shown by F6 formulation. Higher water uptake leads to faster disintegration of tablets. Based on the swelling capacity results shown in Table I, the six disintegrating agents employed in this study were classified into two groups. Pregelatinised starch, sodium starch glycolate, croscarmellose showed large swelling capacity and peanut husk powder, potato starch and crospovidone showed very low swelling capacity. Different types of disintegrating agents might function with different mechanisms of their own. From the above results and discussion, peanut husk powder was found to be a superior disintegrating agent i.e. super-disintegrating agent and the mechanism of disintegration might be due to wicking and high rate of water uptake.[18]

The dissolution studies for Domperidone fast dissolving tablets were conducted for 10 minutes and the cumulative percentage of drug dissolved was shown as a graph in Fig 3. In all the formulations more than half of the labeled drug content was released within first two minutes except formulation F1 and F2. The bursting effect of the super-disintegrating agent present in formulation F3-F6 caused rapid drug release. Almost the total amount of the drug was dissolved within 10 minutes in F5 and F6 formulations containing crospovidone and peanut husk powder respectively. Only 72.30 % of the drug was dissolved in formulation F1 containing potato starch. The dissolution rate of the tablets in the decreasing order was found to be F6 > F5 > F3 > F4 > F2 > F1. These observations were similar to the results of the earlier work carried out on the drug, Ondansetron Hydrochloride and reported from our laboratory.[19] Formulation F6 was found to be the best formulation in the present study.

Table 1: Physical properties of different disintegrating agents.

Name of the Disintegrating agent	Bulk Density (gm/cc)	Tapped Density (gm/cc)	Swelling Capacity (%)
Potato starch	0.451	0.618	27
Pregelatinized starch	0.548	0.798	80
Croscarmellose	0.487	0.776	45
Sodium starch glycolate	0.748	0.886	70
Crospovidone	0.313	0.471	18
Peanut husk powder	0.293	0.458	10

Table 2: Formulae of Domperidone fast dissolving tablets.

Ingredients (mg)	F1	F2	F3	F4	F5	F6
Domperidone	10	10	10	10	10	10
MCC (PH 102)	75	75	75	75	75	75
Lactose	22	22	22	22	22	22
Mannitol	30	30	30	30	30	30
Disintegrating agent	PS 7.5	PGS 7.5	CCS 7.5	SSG 7.5	CP 7.5	PHP 7.5
Aspartame	1	1	1	1	1	1
Sodium lauryl sulphate	1.5	1.5	1.5	1.5	1.5	1.5
Talc	1.5	1.5	1.5	1.5	1.5	1.5
Magnesium stearate	1.5	1.5	1.5	1.5	1.5	1.5
Total	150	150	150	150	150	150

PS= Potato starch PGS= Pregelatinised starch
CCS= Croscarmellose SSG= Sodium starch glycolate
CP= Crospovidone PHP= Peanut husk powder

Table 3: Pre-compression parameters of powder blend.

Formulation	Angle of repose (θ)	Compressibility index (%)	Hausners ratio
F1	25.86±1.70	14.72±1.31	1.21±0.72
F2	30.15±2.08	15.14±1.02	1.24±0.25
F3	29.64±1.24	16.08±1.78	1.22±0.39
F4	28.12±1.55	15.79±1.54	1.17±0.67
F5	26.83±1.93	13.48±1.73	1.14±0.86
F6	24.59±1.09	12.31±1.69	1.13±0.58

Table 4: Post-compression parameters of prepared tablets.

Formulation code	Hardness (kg/cm^2)	Friability (%)	Weight variation (mg)	Drug content (%)
F1	3.7±0.4	0.59±0.6	149.18±2.2	97.25±0.5
F2	3.9±0.5	0.56±0.5	147.89±1.8	98.32±0.6
F3	3.4±0.6	0.69±0.7	150.45±2.5	96.58±0.2
F4	4.2±0.3	0.42±0.4	150.17±2.3	99.76±0.7
F5	3.9±0.4	0.46±0.4	149.26±1.9	96.79±0.4
F6	3.8±0.3	0.55±0.6	148.58±2.5	98.95±0.2

Table 5: Disintegration and wetting properties of prepared tablets.

Formulation code	Disintegration time (sec)	Wetting time(sec)	Water absorption ratio (%)
F1	195.7±8.95	113.8±6.48	94.48±1.65
F2	119.7±7.45	95.4±7.30	94.43±2.24
F3	86.5±5.76	71.8±5.35	95.46±1.46
F4	61.2±4.52	82.8±7.25	97.48±1.78
F5	32.5±6.35	64.7±3.58	96.47±1.42
F6	28.8±5.20	52.8±4.48	98.49±1.54

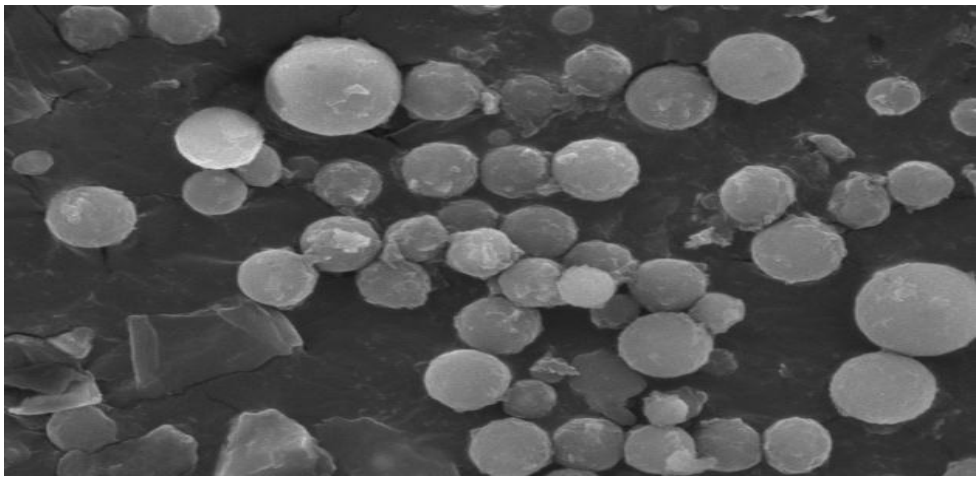

Fig. 1: Surface morphology of peanut husk powder.

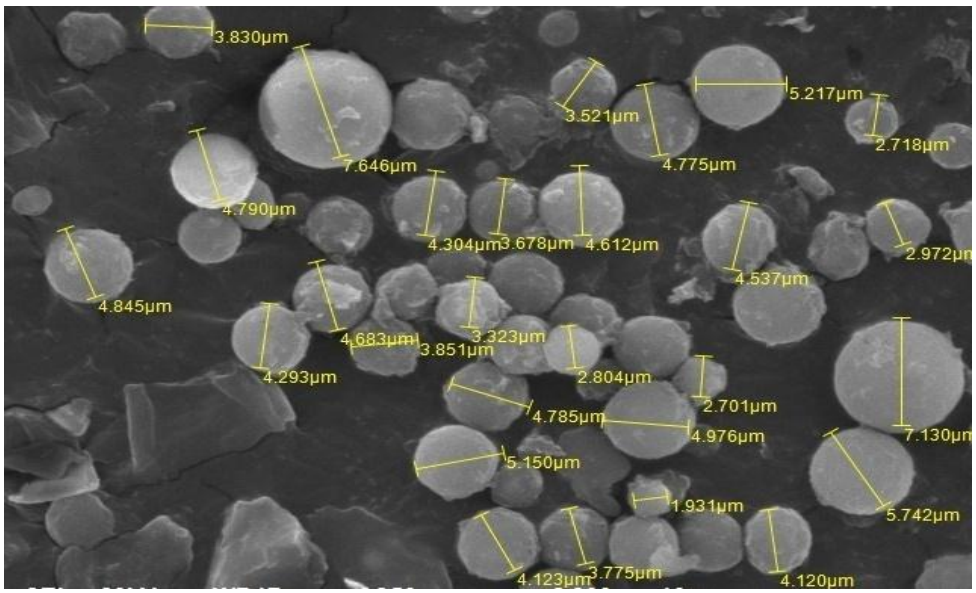

Fig. 2: Size analysis of peanut husk powder.

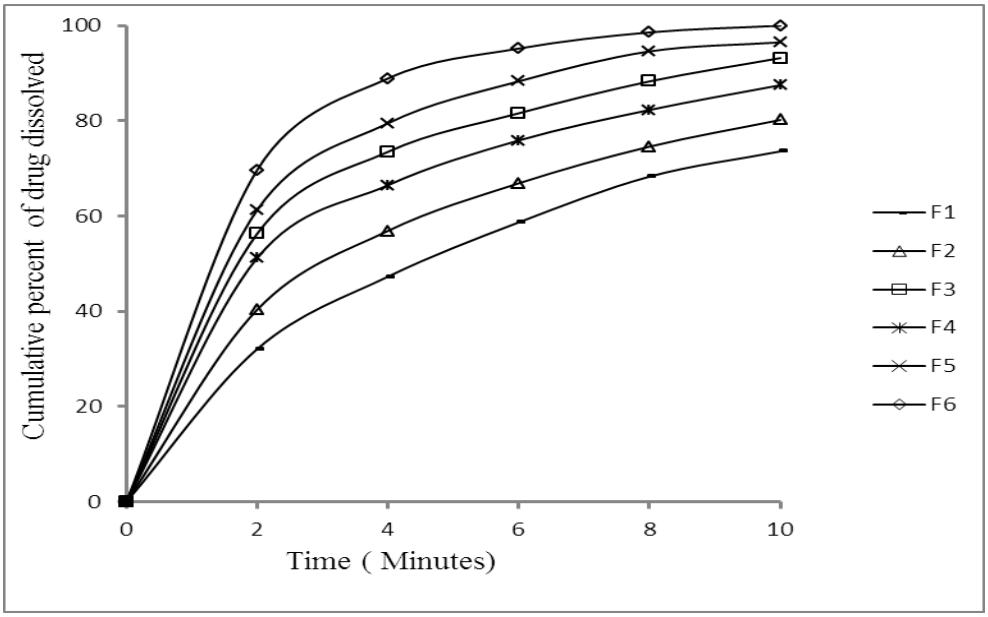

Fig. 3: Dissolution profiles of fast dissolving tablets of Domperidone.

CONCLUSION

Peanut husk powder is a low density powder which is very safe and part of a regular food material. Although it does not show any swelling in water, it is found to be an excellent super-disintegrating agent in the formulation of Domperidone fast dissolving tablets. The mechanism of disintegration action and efficiency of peanut husk powder might be similar to crospovidone, which also does not show any significant swelling property in water. The increase in the dissolution rate of Domperidone enhances its bioavailability and therapeutic efficacy. There is a lot of scope to evaluate this promising new material in further studies in advanced laboratories.

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