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Ocimum Sanctum Seeds, a Natural Superdisintegrant: Formulation and Evaluation of Fast Melt Tablets of Nimesulide

Nasiona bazylii świętej (Ocimum Sanctum) jako naturalny superdezintegrant: wytwarzanie i ocena szybko rozpuszczalnych tabletek Nimesulide

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Summary

Background. Fast melt tablets, also known as fast dissolving tablets, disintegrate instantaneously within the mouth and thus can be consumed without water. The present study was aimed to formulate fast melt tablets of nimesulide by using *Ocimum Sanctum* seeds as a natural tablet superdisintegrant.
Material and Methods. Powdered Ocimum seeds were characterized for powder flow properties (bulk density, tapped density, Carr's consolidation index, Hausner ratio, angle of repose), swelling index, viscosity, pH, loss on drying and microbial load. The prepared tablets were evaluated for different tablet parametric tests, wetting time, water absorption ratio, effective pore radius, porosity, packing fraction, *in vitro* and *in vivo* disintegration time, in-vitro dissolution and stability studies.
Results. The swelling index was evaluated to be 1600. An appreciable effect of the natural material was seen on tablet hardness and friability. The water absorption ratio increased from 56.15 ± 0.85 to 80.76 ± 0.70 (A1–A4). Water uptake coupled natural polymer swelling could be the most probable mechanism for concentration dependent reduction in disintegration time by the *Ocimum Sanctum* seeds. Porosity of the formulated tablets was found to increase from batch A1–A4. The *in vitro* disintegration results were in line with *in vivo* disintegration results. The f_2 values (in comparison with Nimulid MD) of 95.90 and 93.65 were obtained with A3 and A4 batches respectively.
Conclusion. It could be concluded that *Ocimum Sanctum* seeds could be used as a natural superdisintegrant in the formulation of fast melt tablets (**Polim. Med. 2012, 42, 1, 49–59**).

Key words: Superdisintegrant, fast melt tablet, ocimum sanctum, cross carmellose sodium, nimesulide.

Streszczenie

Cel pracy. Szybko rozpuszczalne tabletki znane także jako szybko rozpraszane tabletki ulegają dezintegracji natychmiast w jamie ustnej i dlatego mogą być przyjmowane bez popicia wodą. Prezentowane badanie miało na celu wytworzenie szybko rozpuszczalnych tabletek Nimesulide, z użyciem nasion bazylii świętej (Ocimum Sanctum) jako naturalnego superdezintegrantu tabletki.
Materiał i metody. Sproszkowane nasiona bazylii świętej zbadano pod kątem charakterystyki właściwości przepływu pudru (gęstość masowa, gęstość popychania, indeks konsolidacji carra, współczynnik Hausnera, kąt pokładania), indeksu pęcznienia, lepkości, pH, strat przy wysuszaniu i obciążania mikrobiologicznego. Index pęcznienia określono jako 1600. Przygotowane tabletki przebadano pod kątem różnych testów parametrycznych czasu wilgocenia, wskaźnika absorpcji wody, promienia efektywnego porów, porowatości, frakcji upakowania, czasu dezintegracji *in vitro* i *in vivo*, rozpuszczania *in vitro* i stabilności.
Wyniki. Godne zanotowania właściwości naturalnego materiału zostały zaobserwowane w dziedzinie twardości i sypkości. Wskaźnik absorpcji wody wzrósł od 56,15 ± 0,85 do 80,76 ± 0,70 (A1–A4). Wychwytywanie wody odpowiadało pęcznieniu naturalnego polimeru i może być najbardziej prawdopodobnym mechanizmem redukcji czasu dezintegracji zależnym od stężenia. Porowatość tabletek zwiększała się od partii A1 do A4. Wyniki dezintegracji *In vitro* odpowiadały wynikom *in vivo*. Wartość f_2 (w porównaniu do Nimulidu MD) 95,90 i 93,65 zostały uzyskane odpowiednio w partiach A3 i A4.
Wnioski. Można stwierdzić, że nasiona bazylii świętej (Ocimum Sanctum) mogą być zastosowane jako naturalny superdezintegrant w wytwarzaniu szybko rozpuszczalnych tabletek (**Polim. Med. 2012, 42, 1, 49–59**).

Słowa kluczowe. superdezintegrant, szybko rozpuszczalne tabletki, bazylia święta, nimesulide.

Introduction

Natural ingredients, either active or inactive, are in high demand for their drug delivery applications because of their versatile availability, low cost as compared to synthetic and semi-synthetic products, and their biocompatible and biodegradable nature. Novel drug delivery systems are aimed to produce effective drug therapy with better patient compliance, efficacy and safety. For the systemic action of drugs, the oral route of drug delivery is the most preferred route of administration. The tablet is the most widely used oral dosage form because of its convenience in terms of self-administration and compactness and because it is non-invasive and economical to manufacture. About one third of people, including pediatrics, geriatrics, the bed ridden and old aged patients, face swallowing problems related to solid oral dosage forms which results in poor compliance to drug therapy. Fast disintegrating drug delivery systems, also known as fast melt tablets, offer a solution to overcome the swallowing problems of these patients. Fast melt tablets are commercially prepared by direct compression technology which makes use of superdisintegrants and, when placed on the tongue, disintegrates within seconds, allowing the drug to dissolve or disperse in saliva [1]. The technologies used for the preparation of fast melt tablets include lyophilization [2], molding [3], direct compression [4], the cotton candy process [5], spray drying [6], sublimation [7] and nanonization [8]. The principle behind such techniques is based on increasing the porosity and/or the addition of superdisintegrants and water soluble excipients which aid in the disintegration of the tablets within seconds [9]. Established superdisintegrants such as sodium starch glycolate, cross carmellose sodium and crosspovidone have swelling and capillary-based actions which help in the rapid disintegration of the tablet [10]. Indion 414, an ion exchange resin, has also been discovered for its superdisintegrant properties, which act via a swelling mechanism [11]. Synthetic and semi-synthetic superdisintegrants are prepared from a chemical treatment which increases their cost and ultimately makes the formulation costly. So, there is a vital need of such superdisintegrants which are cost effective and have good superdisintegrant capabilities. Some natural superdisintegrants explored by researchers include *Locust Bean* gum [12], *Plantago Ovata* [13], mango peel pectin [14], *Rhodiola Rosea* [15], *Ocimum Americanum* [16] *Aloe Vera* [17] and *Lallemantia Reylenne* [18].

Nimesulide (4'-nitro-2'-phenoxy methane sulfonanilide) is a weakly acidic, non-steroidal anti-inflammatory drug (BCS class II) which is widely used in the treatment of the management of a variety of painful and inflammatory conditions like post-operative pain, primary dysmenorrhea and painful osteoarthritis. It shows high anti-inflammatory, antipyretic, and analgesic activities in addition to low toxicity, a moderate incidence of gastric side effects, and a high therapeutic index [19].

Several medicinal properties have been attributed to *Ocimum sanctum*. Different parts of the plant e.g. leaves, flowers, stem, root, seeds etc. are known to possess therapeutic potential and have been used traditionally as anti-diabetic, antifertility, hepatoprotective, hypotensive, hypolipidmic, expectorant, analgesic, anticancer, antiasthmatic, antiemetic, diaphoretic and anti-stress agents. Ocimum has also been used in the treatment of fever, bronchitis, arthritis, convulsions, etc. [20].

Ocimum Sanctum seed powder was evaluated for its powder flow properties (bulk density, tapped density, angle of repose, Carr's consolidation index and Hausner ratio), swelling index, loss on drying and microbial load studies. The prepared batches of orodispersible tablets (using an *Ocimum Sanctum* and standard superdisintegrant) were evaluated for parametric tests of tablets (thickness, diameter, hardness, tensile strength and friability), wetting time, water absorption ratio, effective pore radius, porosity, packing fraction, moisture uptake studies, *in vitro* and *in vivo* disintegration time, *in vitro* release and stability studies and similarity factor (f_2) was computed in comparison with the marketed formulation based on *in vitro* release data.

Materials

Nimesulide and cross carmellose sodium were received as gift samples from Park Pharmaceuticals, Baddi, India. Avicel PH-102 was procured from Sigma Aldrich, USA. Sodium Saccharin was purchased from Lobachemie, Mumbai, India. Talc and magnesium stearate were purchased from S. D. Fine Chemicals Ltd. Mumbai, India. *Ocimum Sanctum* seeds were purchased from Yarrow Chem, Mumbai, India. The mango Flavor was purchased from Paras Perfumes, New Delhi, India. The Ocimum Sanctum seeds were powdered and passed through a 60-mesh sieve for use in the research work. All other chemicals and reagents were of analytical grade and were used as such.

Methods

Characterization of *Ocimum Sanctum* seeds

Evaluation of powder flow properties

The powdered seeds were evaluated for flow properties including bulk density, tapped density, angle of repose, Carr's compressibility index and Hausner ratio.

Swelling index

The study was carried out using a 100 ml stoppered graduated cylinder. The initial bulk volume of

1 gm powdered seeds was noted. Water was added in sufficient quantity to produce 100 ml of a uniform dispersion. The sediment volume of the swollen mass was measured after 24 hours and stored at room temperature. The swelling index was calculated as

$$\text{Swelling index} = \frac{V_2 - V_1}{V_1} * 100$$

Where: V_1 andzV_2 are initial volume of material before hydration and volume of hydrated material respectively.

Viscosity

Viscosity of a 1% solution of (w/v) *Ocimum Sanctum* seeds was measured at 37± 1°C using a Searle type viscometer, DV-2 +LV Brookfield Viscometer, USA with spindle number 62 at different rpm.

Determination of pH

The pH of a 1% solution of (w/v) powdered ocimum seeds was determined using a digital pH meter (EI products, India) at 37°C.

Loss on drying

Loss on drying (LOD) is used to determine high levels of moisture or solvents present in the sample. The material sample was weighed (W_1) and heated in an oven for 2 hrs. The sample was cooled in the dry atmosphere of a desiccator, and then reweighed (W_2). % LOD was calculated by

$$\% \text{ LOD} = \frac{(W_1 - W_2)}{W_1} * 100$$

Microbial load

Microbial load was determined as outlined in Indian Pharmacopoeia 2007 for total aerobic count using the plate count method. A pre-treated sample was inoculated on nutrient agar plates and were incubated for 96 hours and 120 hours at 34 ± 0.5°C and 22 ± 0.5°C for bacteria and fungi respectively. Then the number of colony forming units was calculated for bacteria and fungi.

Preparation of tablets

Fast melt tablets containing 100 mg of nimesulide were prepared by direct compression method and the different formulae employed in the study are shown in table 1. The drug and excipients were passed through 60 mesh sieve to ensure better mixing. Avicel PH 102 was used as a directly compressible diluent. The directly compressible mixtures were compressed using a multi-punch tableting machine (AK Industries, India) fitted with an 8.40 mm flat-faced punch and die set possessing 50 tons of compression force. About 300 tablets were made for each batch.

Evaluation of tablets

Diameter and thickness

A calibrated vernier caliper (Indian caliper industries, Ambala, India) was used to evaluate diameter and thickness of tablets.

Hardness

The hardness of the tablets was determined by using a Monsanto hardness tester (Pharma Chem Machineries, Mumbai, India). A tablet hardness of about 4–5 kg/cm^2 is considered adequate for mechanical stability.

Friability

As per USP 30-NF 25, twenty six tablets were taken which corresponded to 6.5 g weight. The tablets were placed in a Roche friabilator and were rotated at 25 rpm for 4 minutes. The tablets were taken out, dedusted and reweighed. The percentage friability of the tablets was calculated by the formula

$$\text{Percentage friability} = \frac{\text{Initial weight} - \text{Final weight}}{\text{Initial weight}} \times 100$$

Tablet tensile strength

The tablet tensile strength is the force required to break a tablet by compressing it in the radial direction and is measured using a Monsanto hardness tester. For measuring the hardness of the tablets, the plunger of the hardness tester is driven down at a speed of 20 mm/min. Tensile strength for crushing (T) is calculated using the equation:

$$T = 2F/\pi dt$$

Where: F is the crushing load, and d and t signify the diameter and thickness of the tablet respectively.

Weight variation test

20 tablets from each batch were subjected to a weight variation test. As per Indian Pharmacopoeia standards, the tablets should be within the specified limits i.e. ± 5% of average weight.

Wetting Time

A piece of tissue paper (10.75 × 12 mm) folded twice was placed in a culture dish (d = 6.5 cm) contain-

ing 6 ml of simulated saliva (phosphate buffer pH 6.8). A tablet was carefully placed on the surface of tissue paper and the time required for simulated saliva to reach the upper surface of the tablet was noted as the wetting time [21].

Water Absorption Ratio

A test was done with the same procedure as that of wetting time. In this test, initial weight of the tablet was noted before placing it on a Petri dish. After complete wetting, the wetted tablet was then weighed. The water absorption ratio, R, was determined using the equation,

$$R = 100\ (W_a - W_b)/W_b$$

Where: W_a is weight of the tablet after water absorption and W_b is weight of the tablet before absorption [21].

Effective pore radius ($R_{eff.P}$)

$R_{eff.P}$ of the powder blend was determined using the method reported by Rana et al. [22] In short, a micropipette tip (2 ml, transparent) was completely filled with powder and weighed (W_i). Then n-hexane (surface tension (γ) 18.4 mN/m) was poured dropwise on the bedtop till the solvent filtered out at the bottom of the tip. The tip was reweighed (W_f). The experiments were repeated 3 times.

$$R_{eff.P} = W_f - W_i/2\pi\gamma$$

Porosity

Porosity is a measure of the void spaces in a material, and is a fraction of the volume of voids over the total volume. Its value ranges between 0–1, or as a percentage between 0–100.

The porosity of the tablets was calculated as follows:

$$\epsilon = 1 - \frac{m}{\rho^{*}_{true} V}$$

Where: ρ_{true} is the true density of the mixture, m and V are the weight and volume of the tablet, respectively. The true density of the powder was determined using a true density meter (SMART PYCNO 30). Initially a vacuum is necessary to remove air from the pores of the sample after which purging with Helium gas is done. Then the normal procedure is followed. Two pressure readings were used to calculate true density. Initially helium gas was pressurized in a known reference volume. This reading was taken as the first pressure reading. Then the gas was allowed to pass to a sample cell containing the sample material which resulted in a pressure drop as compared to initial pressure and this dropped pressure was taken as the second pressure reading. Then material volume was calculated from which true density was determined.

Tablet packing fraction

The tablet packing fraction (P_f) is a measure of the degree of consolidation or compactness of the tablet. Tablet packing fraction was determined by the following method:

$$\text{Packing fraction } (P_f) = w/\pi r^2 t\rho$$

Where w is the weight of a tablet, r is radius, t is thickness and ρ is the particle density.

Ten tablets were used in each measurement. The radius and thickness of the tablets were measured using a vernier caliper. The apparent particle density of the drug powder was determined using the liquid paraffin displacement method. Firstly, the weight of a specific gravity (SG) bottle filled with liquid paraffin and the weight of the SG bottle containing a sample of the drug powder (1 g) was noted. Then the SG bottle was filled with liquid paraffin. The final weight was determined. The determination was performed in triplicate, and mean results were used in the calculation of P_f. If the packing fraction is very high, fluid is unable to penetrate into the tablet which leads to slower disintegration [23].

In vitro disintegration time

Disintegration time for fast melt tablets was determined using USP disintegration apparatus with simulated saliva (Phosphate buffer pH 6.8, 900 ml at 37°C) as the disintegrating medium. To comply the test, all tablets should disintegrate within 3 minutes as per official requirements.

In vivo disintegration time

Five healthy male volunteers were selected for determination of in vivo disintegration time. The volunteers were previously informed about the purpose of the study. Initially, all of the volunteers were instructed to rinse their oral cavity with distilled water after which they were instructed to place one tablet on the tongue. A stopwatch was started immediately. Volunteers were strictly told not to chew or swallow the tablets, licking was allowed. The test was finished when there were no lumps left in the oral cavity, after which the volunteers were told to rinse their mouth properly.

Moisture uptake studies

Due to the high content of hydrophilic excipients, fast melt tablets have an increased chance of moisture uptake which greatly affects stability of moisture sensi-

tive products. So, there is a need for special attention towards storage and packaging of fast melt tablets. Therefore, moisture uptake studies are strongly recommended for fast melt tablets [24]. The test was performed by keeping ten tablets in a desiccator (containing calcium chloride) for 24 hours at 37ºC to assure complete drying. The tablets were then weighed and stored for 2 weeks at 75% humidity. To achieve required humidity, a saturated solution of sodium chloride was kept at the bottom of the desiccator for three days. On the tenth day, the tablets were re-weighed and the percentage increase in the weight was recorded.

Drug content

Twenty tablets were weighed and powdered. An amount of the powder equivalent to 100 mg of nimesulide was dissolved in 100 ml of pH 8.4 alkaline borate buffer, filtered, diluted appropriately and analyzed for drug content at 397 nm using UV-Visible spectrophotometer (Systronics 2202, India).

In vitro dissolution Studies

For *in vitro* drug release studies, an eight stage USP dissolution apparatus II (Lab India, DS 8000) was used. The dissolution test was performed using 900 ml of alkaline borate buffer (pH 8.4) at 37 ± 0.5°C. The speed of the rotation of paddle was set at 100 rpm. At a predetermined time interval, 5 ml samples were withdrawn, filtered through Whatman filter paper, adequately diluted and analyzed using a UV-Visible spectrophotometer (Systronics 2202) at 397 nm. All experiments were run in triplicate.

Stability testing

The prepared batches were evaluated for stability studies. During the full duration of study, temperature and relative humidity of about 40 ± 2°C and 75% RH respectively were maintained. The formulations were analyzed at 0 day, 1 and 3 month time intervals for hardness, friability, tensile strength, drug content and in vitro disintegration time.

Results and discussion

Characterization of *Ocimum Sanctum* seeds

Powder flow properties, swelling index, viscosity, pH, loss on drying (LOD) and microbial load were studied for characterizing the powdered *Ocimum Sanctum* seeds. The results of powder flow properties (Table 2) clearly indicate good flow characteristics. The swelling index was found to be 1600 which point towards good swelling capability of *Ocimum Sanctum* seeds. Viscosity of 1% w/v solution at 37 ± 1°C of seeds of *Ocimum Sanctum*, using spindle number 62 of a Brookfield viscometer, was found to be 6, 4.5, 4, and 3.3 at 10, 20, 50 and 100 rpm respectively and a plot of shear stress v/s rate of shear was obtained (figure 1) which clearly indicate adherence to the Newtonian behavior. A powdered ocimum seed solution (1%w/v) at 37 ± 1°C exhibited a pH of 6.2. Loss on drying was obtained to be 9.55%. As natural materials are prone to possess microbial contamination, so it becomes necessary to perform microbial load studies. Total aerobic count using the plate count method was determined as given in Indian Pharmacopoeia 2007 (figure 2). The number of colony forming units were found to be 52 CFUs/g and 5 CFUs/g for bacteria and fungi respectively which were well within limits as per Indian Pharmacopoeia 2007 for total aerobic count.

Evaluation of tablets

All the batches of fast melt tablets were formulated under similar conditions to avoid processing variables.

Table 1. Composition of Nimesulide fast melt tablet formulations

Ingredients (mg)	A1	A2	A3	A4	B1	B2	B3	B4
Nimesulide	100	100	100	100	100	100	100	100
Ocimum Sanctum powder	6.25	12.5	18.75	25	–	–	–	–
Crosscarmellose sodium	–	–	–	–	6.25	12.5	18.75	25
Orange Flavor	5	5	5	5	5	5	5	5
Sodium Saccharin	2.5	2.5	2.5	2.5	2.5	2.5	2.5	2.5
Avicel PH 102	131.55	125.0	118.75	112.5	131.55	125.0	118.75	112
Talc	2.5	2.5	2.5	2.5	2.5	2.5	2.5	2.5
Magnesium stearate	2.5	2.5	2.5	2.5	2.5	2.5	2.5	2.5
Total weight	250	250	250	250	250	250	250	250

Table 2. Powder evaluation parameters

Parameters	Results
Bulk Density(g/cm^3)	0.74
Tapped density(g/cm^3)	0.57
Carr's compressibility index (%)	22.11
Angle of Repose	20.80
Hausner Ratio	1.29
Swelling index	1600
pH	6.2
LOD (%)	9.55

The tablets prepared by direct compression method were found to be free from capping, chipping and sticking. The prepared tablets were evaluated for various physical parametric tests. The diameter and thickness (Table 3) of the tablet batches were found to range between 8.40 ± 0.06 to 8.42 ± 0.05 mm (A1–A4), 8.43 ± 0.04 to 8.46 ± 0.02 and 4.74 ± 0.02 to 4.78 ± 0.04 mm (A1–A4), 4.81 ± 0.06 to 4.80 ± 0.05 mm, respectively. An appreciable effect was seen on tablet hardness, friability and tensile strength due to increasing concentration of Ocimum seeds. Hardness and friability (figure 3) were found to be 2.95 ± 0.66 to 4.63 ± 0.35 kg/cm^2 and 0.55 ± 0.05 to 0.26 ± 0.07%, respectively, clearly indicating the binding potential of *Ocimum Sanctum* seeds. Tensile strength (a parameter of mechanical integrity of the tablets) was found to increase from 0.471 ± 0.08 to 0.733 ± 0.10 MN/m^2, respectively, confirming the binding capability of *Ocimum Sanctum* seeds. All of the batches passed a weight variation test.

Wetting time, water absorption ratio and in-vitro disintegration time were found to range between 38 ± 1

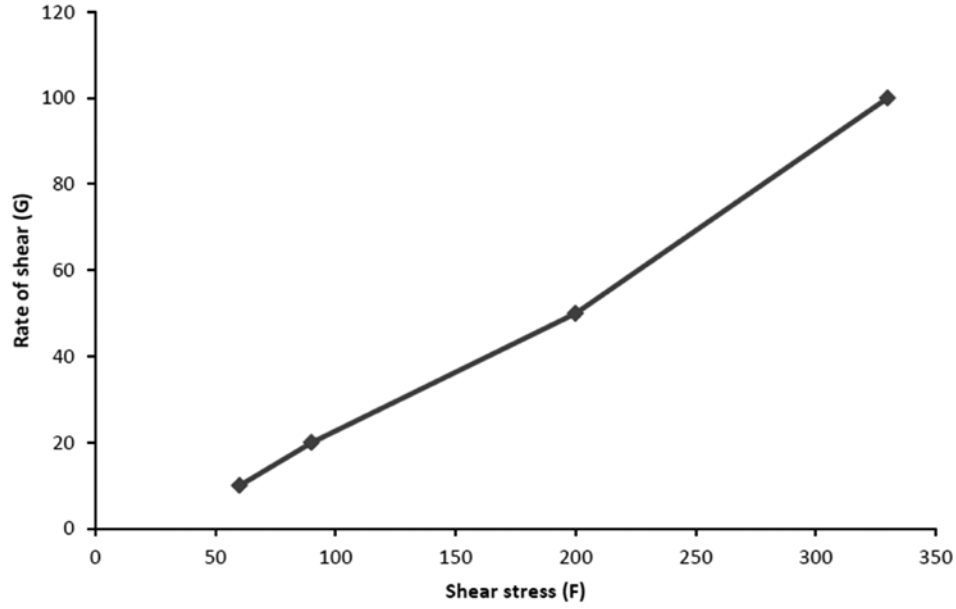

Fig. 1. Shear stress versus rate of shear plot

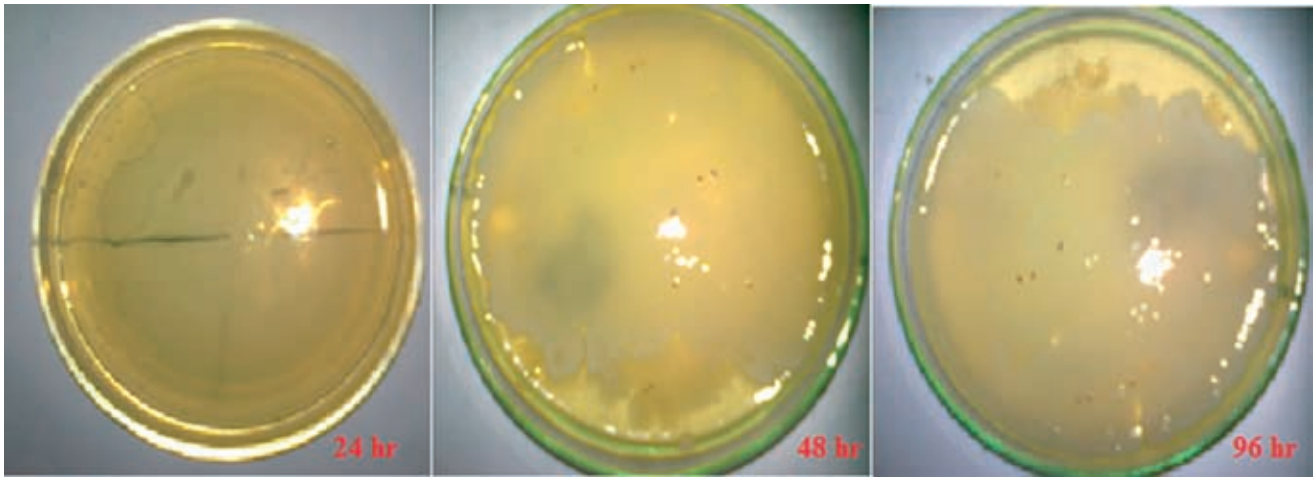

Fig. 2. Microbial load studies

Table 3. Evaluated of the prepared tablets

Parameters	A1	A2	A3	A4	B1	B2	B3	B4
Diameter (mm)	8.40 ± 0.06	8.45 ± 0.03	8.41 ± 0.02	8.42 ± 0.05	8.43 ± 0.04	8.41 ± 0.02	8.42 ± 0.05	8.46 ± 0.02
Thickness (mm)	4.71 ± 0.03	4.75 ± 0.04	4.73 ± 0.02	4.78 ± 0.04	4.81 ± 0.06	4.79 ± 0.07	4.80 ± 0.02	4.80 ± 0.05
Friability (%)	0.55 ± 0.05	0.46 ± 0.05	0.40 ± 0.01	0.26 ± 0.07	0.84 ± 0. 06	0.87 ± 0.04	0.70 ± 0.02	0.68 ± 0.01
Hardness (kg/cm^2)	2.95 ± 0.66	3.20 ± 0.37	3.91 ± 0.52	4.63 ± 0.35	2.56 ± 0.72	2.87 ± 0.49	3.01 ± 0.77	3.40 ± 0.56
Tensile strength (MN/m^2)	0.471 ± 0.08	0.507 ± 0.12	0.622 ± 0.05	0.733 ± 0.10	0.402 ± 0.09	0.454 ± 0.07	0.475 ± 0.14	0.537 ± 0.11
Weight variation test	Pass	Pass	Pass	Pass	Pass	Pass	Pass	Pass
Wetting time (sec)	38 ± 1	30 ± 2	22 ± 1	12 ± 3	51 ± 2	44 ± 4	38 ± 1	36 ± 3
Water absorption ratio %	56.15 ± 0.85	63.52 ± 1.01	66.66 ± 0.54	80.76 ± 0.70	52.12 ± 0.66	59.10 ± 0.28	63.29 ± 1.45	70.53 ± 1.10
In-vitro disintegration time (sec)	40 ± 2	28 ± 1	15 ± 2	10 ± 1	65 ± 5	55 ± 4	40 ± 6	25 ± 5
In-vivo disintegration time (sec)	42 ± 1	30 ± 3	17 ± 2	12 ± 2	63 ± 5	52 ± 6	42 ± 3	27 ± 2
Moisture uptake (%)	0.92 ± 0.05	0.96 ± 0.05	1.15 ± 0.02	1.34 ± 0.05	0.47 ± 0.01	0.55 ± 0.01	0.62 ± 0.04	0.77 ± 0.02
Drug content (%)	99.84 ± 0.25	98.12 ± 0.29	97.85 ± 0.66	98.12 ± 0.45	95.75 ± 1.03	96.59 ± 0.56	98.22 ± 0.87	97.27 ± 0.92
f_2	69.67	82.01	95.90	93.65	71.13	87.55	81.49	71.80

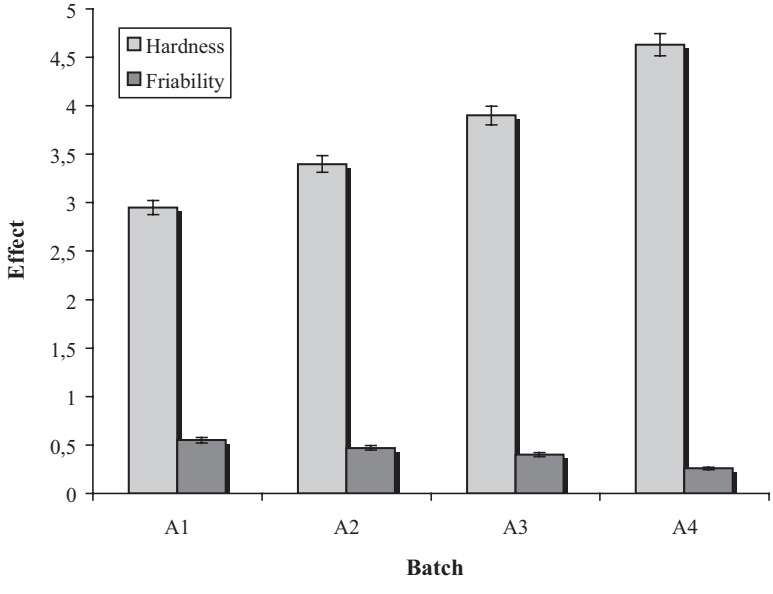

Fig. 3. Effect of *Ocimum Sanctum* on tablet hardness and friability

to 12 ± 3 seconds, 56.15 ± 0.85 to 80.76 ± 0.70 and 40 ± 2 to 10 ± 1 seconds, respectively. Water absorption capacity was found to increase with the increase in concentration of *Ocimum Sanctum* seeds from batches A1 to A4 which could be due to higher water uptake by the natural polymer. Formation of highly wettable/porous structures upon contact with water may be the best possible reason for the fast disintegration achieved by the addition of *Ocimum Sanctum* seeds in the fast melt tablets. $R_{eff.P}$ (effective pore radius) is an indicator of tablet porosity. $R_{eff.P}$ and porosity (Figure 4 and 5) were found to range from 2.94 ± 0.23 to 4.12 ± 0.14 mm (A1 to

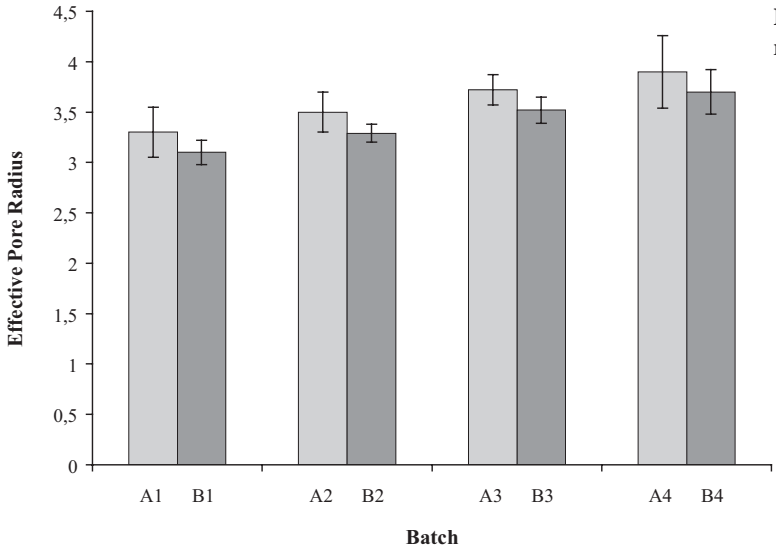

Fig. 4. Effect of *Ocimum Sanctum* on effective pore radius

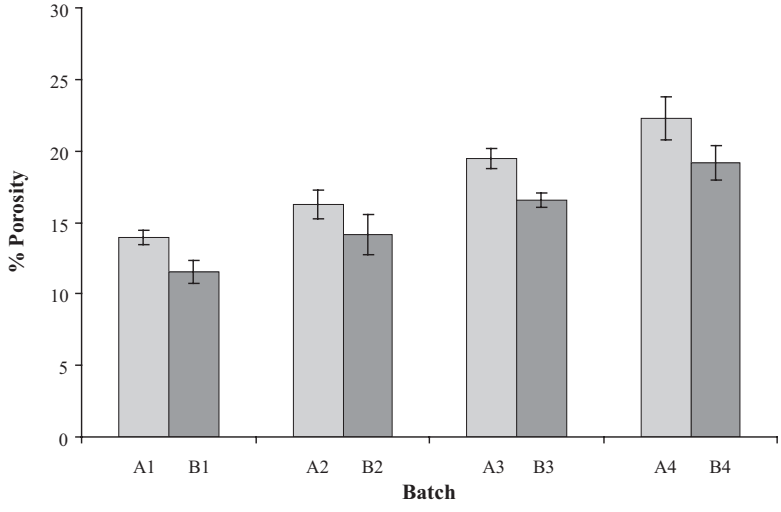

Fig. 5. Effect of *Ocimum Sanctum* on tablet porosity

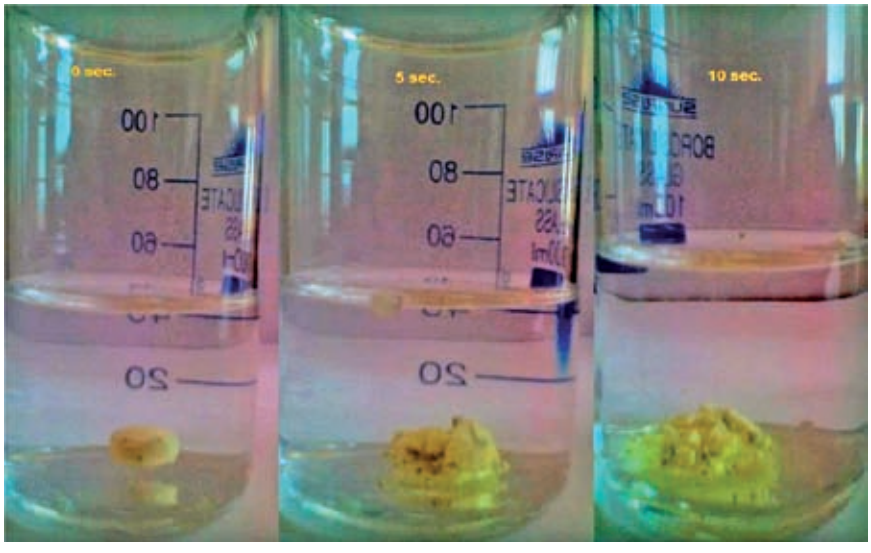

Fig. 6. Disintegration pattern of prepared orodispersible tablets containing *Ocimum Sanctum* seeds

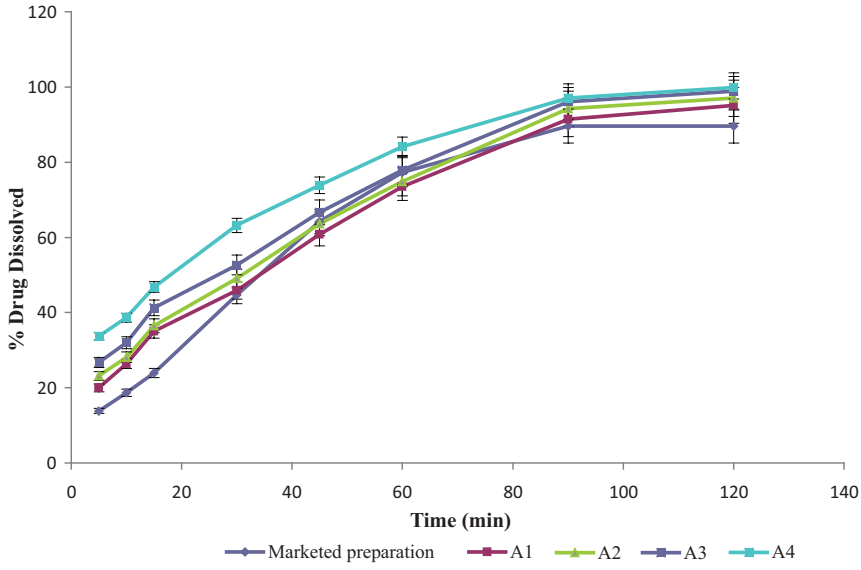

Fig. 7. *In vitro* release profile of Nimesulide from fast melt tablets prepared using powdered *Ocimum Sanctum* seeds as a superdisintegrant

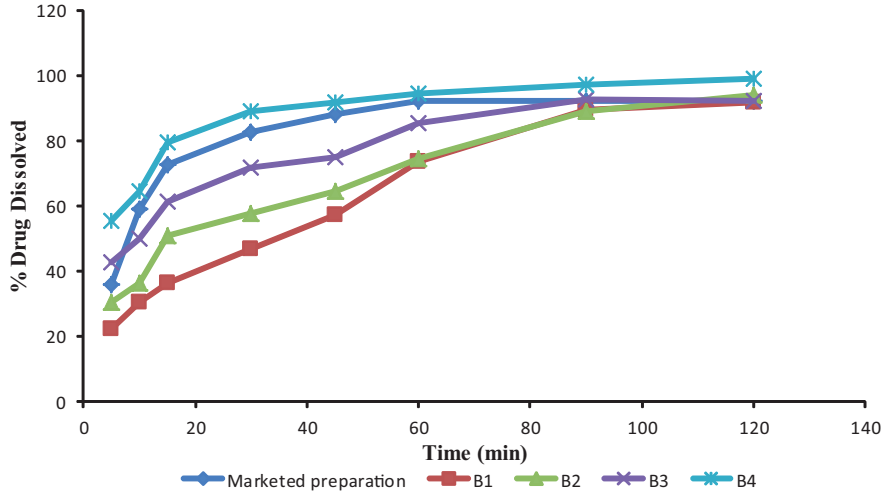

Fig. 8. *In vitro* release profile of Nimesulide from fast melt tablets prepared using crosscarmellose sodium as a superdisintegrant

A4) and 13.99 to 22.231%, respectively, indicating an appreciable ability of *Ocimum Sanctum* seeds to increase water penetration due to a wicking action which increases tablet porosity and thus lowers disintegration time. The tablet packing fraction was found to be 0.856, 0.825, 0.792 and 0.772 (A1–A4) which indicates the tablet superdisintegrant property of *Ocimum Sanctum* seeds. Figure 6 depicts the disintegration pattern of fast melt tablets formulated using *Ocimum Sanctum* seeds as a superdisintegrant. *In vivo* disintegration time was judged on five healthy male volunteers. The *in vivo* disintegration time was found to be 42 ± 1 to 11 ± 2 seconds (A1–A4). As evident from the results, *in vitro* results were well in line with the *in vivo* results.

The moisture uptake study indicated no significant uptake of moisture by the prepared batches during the 10 day trial period. Percent moisture uptake was found to be 0.92 ± 0.05 to 1.34 ± 0.05 (A1–A4) and 0.47 ± 0.07 to 0.77 ± 0.02 (B1–B4).

In vitro nimesulide release was 90.56% (A1), 97.01% (A4), 91.58% (B1) and 94.21% (B4) in batches of fast melt tablets (Figure 7 and 8). The similarity factor (f_2) is a logarithmic transformation of the sum-squared error of differences between test T_j and reference R_j products over all time points. It is a useful tool for comparison of dissolution profiles when more than three or four dissolution time points are available.

$$f_2 = 50 \text{ x } \log\{[1+(1/n)\sum_{j=1}^{n} w_j \left|R_j - T_j\right|^2]^{-0.5} \text{ x } 100\}$$

Where: w_j is an optional weight factor. The similarity factor fits result between 0 and 100. It is 100 when the test and reference profiles are identical and tends to 0 as the dissimilarity increases. In order to consider similar dissolution profiles, f_2 values should be close to 100. The results obtained from the calculation of the f_2

Table 4. Stability study data of orodispersible tablets

Batch	Parameter (Months)														
	Hardness (Kg/cm^2)			Friability (%)			Tensile strength (MN/m^2)			Drug content (%)			In-vitro disintegration time (sec.)		
	0	1	3	0	1	3	0	1	3	0	1	3	0	1	3
A1	2.95 ± 0.60	2.75 ± 0.25	2.55 ± 0.40	0.55 ± 0.05	0.61 ± 0.10	0.65 ± 0.30	0.471 ± 0.08	0.449 ± 0.05	0.432 ± 0.02	99.24 ± 0.15	98.55 ± 0.10	97.99 ± 0.25	40 ± 2	42 ± 1	45 ± 1
A2	3.20 ± 0.30	3.10 ± 0.10	3.00 ± 0.50	0.46 ± 0.05	0.51 ± 0.10	0.55 ± 0.15	0.507 ± 0.12	0.498 ± 0.20	0.490 ± 0.30	98.78 ± 0.10	98.45 ± 0.25	98.89 ± 0.45	28 ± 1	30 ± 2	31 ± 2
A3	3.91 ± 0.52	3.85 ± 0.15	3.80 ± 0.22	0.40 ± 0.01	0.45 ± 0.15	0.49 ± 0.25	0.622 ± 0.05	0.610 ± 0.10	0.590 ± 0.15	97.98 ± 0.25	97.72 ± 0.10	96.85 ± 0.16	15 ± 2	17 ± 3	19 ± 1
A4	4.63 ± 0.35	4.55 ± 0.25	4.50 ± 0.10	0.26 ± 0.07	0.29 ± 0.45	0.35 ± 0.20	0.733 ± 0.10	0.720 ± 0.13	0.705 ± 0.14	98.12 ± 0.22	97.85 ± 0.12	97.15 ± 0.23	10 ± 1	13 ± 1	14 ± 2

factor showed that there is a similarity of dissolution profiles between A1 to A4 and B1 to B4 and Nimulid MD tablets. However A3 and A4 batches showed f_2 values of 95.91 and 93.65, respectively, which were highest amongst all the formulated batches.

Stability studies for the prepared batches of fast melt tablets containing *Ocimum Sanctum* seeds as a superdisintegrant revealed that there was no significant change in tablet hardness, friability, tensile strength, drug content and in-vitro disintegration time (Table 4).

Conclusion

In the present study, the superdisintegrant property of *Ocimum Sanctum* seeds have been explored. The tablets disintegrated much faster and consistently when ocimum seeds were used as a superdisintegrant compared with cross carmellose sodium. It can be concluded that *Ocimum Sanctum* seeds could be used as a natural superdisintegrant in the formulation of fast melt tablets.

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