An Elsevier Indexed Journal ISSN-2230-7346

Journal of Global Trends in Pharmaceutical Sciences

FORMULATION AND EVALUATION OF ORODISPERSIBLE TABLETS USING A NATURAL POLYSACCHARIDE ISOLATED FROM THE RAW FRUITS OF *HIBISCUS SABDARIFFA*

Gana Manjusha Kondepudi*, Bala Krishnaiah P, G L D Manvi, D Hemasundararao, B Sudha Chandan, Gummadi Bhargav

Vignan Institute of Pharmaceutical Technology, Duvvada, Visakhapatnam, Andhra Pradesh, India-530049.

*Corresponding author E-mail: **manjusha.kondepudi.g@gmail.com**

ARTICLE INFO

Key Words

ODTs,
Diclofenac sodium
H. sabdariffa

Access this article online
Website:
https://www.jgtps.com/
Quick Response Code:

ABSTRACT

Among all the dosage forms, solid dosage forms are more compliant to patients with tablets on top because of the ease of administration and minimal dose. However geriatric and pediatric patients experience difficulty in swallowing of tablets, resulting in poor adherence. Orodispersible tablets (ODTs) can be an answer to the poor compliance because ODTs dissolve and disintegrate immediately in patient's buccal cavity. The ODTs formulated with natural polymers have more demand than those manufactured from synthetic polymers because natural polymers are non toxic, biodegradable and chemically inert. Objective: In the present study, a polysaccharide was isolated from the raw fruits of *Hibiscus sabdariffa* was investigated as a super disintegrant in the development of orodispersible tablets. Materials and Methods: Diclofenac sodium tablets were prepared separately using various concentrations (1%, 2.5%, 5%, 7.5% w/w) of isolated *H. sabdariffa* raw fruit polysaccharide (natural) and sodium starch glycolate (synthetic) as super disintegrant by the direct compression method. The pre and post compression parameters were evaluated for the prepared tablets. Stability studies were conducted on the optimized formulation (F4). FTIR studies were conducted to characterize drug excipient compatibility. Results: The formulation F4 containing 7.5 % of polysaccharide showed good wetting time when compared to formulation containing sodium starch glycolate at the identical concentration level. Hence it is considered as optimized formulation. Conclusion: The current study revealed the potential of *H. sabdariffa* as disintegrant within the formulation of ODTs. Utilization of *H.sabdariffa* raw fruits for isolation of polysaccharide serve two purposes, waste management and as an alternative source for current synthetic polymers.

INTRODUCTION

Tablets and capsules are most acceptable of all the oral dosage forms because of the compactness, dosage precision and least content variability. Tablets and capsules are not so popular amongst elderly and children as they often experience difficulties in swallowing. The Problem of dysphagia can be solved and compliance can be improved by developing tablets that can dissolve fast in the patient's buccal mucosa eliminating the need to swallow. This led to the development of novel dosage forms called orodispersible tablets

(ODTs). Rapid melt tablets, fast or mouth dissolving tablets are the synonyms of orodispersible tablets[1]. ODTs disintegrate quickly in the patient's mouth. Because of the shorter disintegration time of ODT; there will be fast release of active ingredients and increased bioavailability. Orodispersible tablets can be used with ease while travelling or when there is no access to water[2]. Hence Orodispersible tablets can be conveniently used for pediatric, geriatric patients, pregnant women and patients with dysphagia. The speed of disintegration can be attributed to the properties of the disintegrant used in tablet formulation. The time of disintegration can be rapidly enhanced by the use of super disintegrants. Croscarmellose sodium, sodium starch glycolate, crospovidone are most commonly used synthetic super disintegrants. Various natural substances like starch, gum karaya, agar and their modified forms are also used in the development of orodispersible tablets. There is always a huge demand ad interest for substances of natural origin as pharmaceutical excipients. This is because of their abundant availability, non irritating and non toxic nature. Natural excipients also offer other advantages over synthetic excipients such as ease of isolation, local availability and biocompatibility[3]. The advent of science and technology helps in the conversion of agro industrial wastes in to value added products. Among these value added products, natural polymers occupied a prominent place due to their versatile pharmaceutical applications[4]. Gums and mucilage are on the top among the natural the polymers. *Hibiscus sabdariffa* L (Family: Malvaceae) also known as roselle is widely cultivated in tropical and sub tropical countries. Its leaves are eaten; calyces are used in the making of herbal teas, jams, jellies and other confectionaries. Stems are used for fibre. Generally fruits are thrown as wastes after the leaves are harvested. *H. sabdariffa* is also used for many medicinal properties such as antiseptic, astringent, aphrodisiac, cholagogue, demulcent, digestive, purgative, sedative, stomachic and tonic[5]. *H. sabdariffa* fruits are rich in various phytochemicals such as pectin, ascorbic acid, calcium oxalate, α-terpenyl acetate, anisaldehyde, caprylic acid and minerals. The raw fruits of *H. sabdariffa* are mucilaginous and the pH of the raw fruit mucilage is approximately 7. A thorough literature survey revealed that *H. sabdariffa* polysaccharide is not isolated till date and is used as pharmaceutical excipeint. Hence the present study deals with the isolation of mucilage from the raw fruits of *H. sabdariffa* and investigation of isolated mucilage as disnitegrant in the formulation of orodispersible tablets and comparison of its disintegrating potential with synthetic superdisintegrants. Diclofenac sodium is the model drug taken. The present research work is aimed at the development and evaluation of orodispersible tablets of diclofenac sodium using a polysaccharide isolated from *H. sabdariffa* in order to produce rapid onset of action and improved patient compliance.

METHODS

Materials

All materials used in this present research were of commercial samples. Diclofenac sodium (Yarrow chem. Products, Mumbai), Microcrystalline cellulose (Chemica- biochemica reagents, Mumbai), Sodium starch glycolate (Yarrow chem. Products, Mumbai), Sodium saccharin (Yarrow chem. Products, Mumbai), Vanilla (Yarrow chem. Products, Mumbai), Magnesium Stearate (Yarrow chem. Products, Mumbai), Talc (Yarrow chem. Products, Mumbai). All other chemicals were of analytical reagent grades.

Isolation of polysaccharide from fruits of *H. sabdariffa:* The raw and unripe fruits of *H. sabdariffa* were milled and mixture was soaked in distilled water for 4-5 hours. The viscous solution obtained was strained through a muslin cloth. The polysaccharide was obtained by precipitation method with the addition of acetone (1:4) under continuous stirring. The precipitated polysaccharide was transferred to an evaporating dish and treated consecutively with acetone. The polysaccharide obtained was dried in oven at 40–45 °C. It was then powdered and passed through sieve number 60 and stored in an airtight container. The isolated polysaccharide was characterized for various physicochemical properties such as solubility,

pH (1% w/w in water), swelling index, loss on drying, ash value, bulk and tapped density, compressibility index, Hausner's ratio, and angle of repose as per the reported methods[6,7].

Formulation of Orodispersable tablet: ODTs of Diclofenac sodium were prepared by the direct compression method using isolated polysaccharide and synthetic superdisintegrant at concentration of 1, 2.5, 5, 7.5% w/w. All the ingredients were passed through 60 mesh sieve. Weighed quantity of each ingredient was taken and the blend (Powder mix) was uniformly mixed and compressed into tablets of 200mg using rotary tablet compression machine (Elite Scientifics). The composition of each formulation is given in table 1.

***Evaluation of powder blend (Pre-compression parameters)*:** The powder mix was evaluated for various flow properties such as angle of repose, bulk and tapped density, Hausner's ratio and Carr's index.

Angle of repose: The angle of repose of powder was carried out by the fixed funnel method. The accurately weighed quantity of powder mix was taken in a funnel. The height of the funnel was maintained in such a way that the tip of the funnel just touched the apex of the heap of the powder. The powder was allowed to flow through the funnel without any resistance on to the surface. The diameter and height of the powder cone was measured. Angle of repose was determined using subsequent equation: $\text{Tan } \Theta = h/r$

Where, h and r are the height and radius of the powder cone.

Bulk density and tapped density

Powder weighing 5g from each formula was introduced into a 25-mL measuring cylinder. It was initially shaken lightly to break any agglomerates formed. Initial volume was noted and cylinder was allowed to fall under its own weight onto a hard surface from the height of 2.5cm at 2-second intervals. The tapping was continued until a constant volume was observed. LBD and TBD were calculated using the following formulas: LBD = Weight of the powder/volume of the packing. TBD = Weight of the powder/tapped volume of the packing

Compressibility index and Hausners ratio

The following formula was used to determine the compressibility index of granules: Carr's compressibility index (Carr's index) = {(TBD – LBD) × 100]/TBD

Hausner's ratio was calculated by the following formula: Hausner's ratio = Tapped density / Bulk density

Evaluation of tablets (Post compression parameters)

Tablet hardness: Hardness is a vital parameter which prevents breakage of tablets during transportation, handling and storage. The hardness of tablet was measured by Monsanto hardness tester and was expressed in terms of Kg/cm^2

Tablet thickness: The tablet was placed between the two arms of the Vernier Caliper and thickness was determined. Five measurements were taken.

Weight variation: Twenty tablets were selected arbitrarily from each formulation and weighed individually using a digital balance. The individual weights were noted and compared with the average weight for the weight variation[8].

Friability: Twenty tablets were weighed then they were placed in a plastic chambered friabilator USP type Roche friabilator (Pharmalab, Ahmedabad, India) attached to a motor revolving at a speed of 25 rpm for 4 min. The tablets were reweighed and percentage weight loss (friability) was calculated using the following formula. Friability = [(Initial weight-Final weight) / (Initial weight)]×100%

Drug content: Ten tablets were weighed and crushed to a fine powder, a quantity of powder equivalent to 40 mg to Diclofenac sodium was introduced into 100mL volumetric flask and extracted using PH 6.8 phosphate buffer. The solution obtained was filtered and the filtrate was suitably diluted with pH 6.8 phosphate buffer. The Diclofenac sodium content was determined by measuring the absorbance at 250 nm using UV-Visible Spectrophotometer (Shimadzu 1800).

The drug content was determined using standard calibration curve. The mean percent drug content was calculated as an average of three determinations[9].

Wetting time and water absorption ratio(R)

A tissue paper was taken and folded twice and placed in a Petri dish having an internal diameter of 5 cm containing 6 ml of water. A tablet was cautiously placed on the top of the tissue in the Petri dish. Wetting time was noted as the time required for water to reach the upper surface of the tablet and to completely wet it[10]. Water absorption ratio (R) was then determined according to the following equation: $R = 100 \times (wa - wb)/wb$

Where 'wb' and 'wa' were tablet weights before and after water absorption, respectively.

***In vitro* disintegration time:** The tablet disintegration test apparatus was used to determine disintegration time for all formulations. Six tablets were placed individually in each tube of disintegration test apparatus. The medium was maintained at a temperature of $37^o \pm 2^oC$ and time was noted for the entire tablet to disintegrate completely.

***In-vitro* dissolution:** USP dissolution test apparatus (Electro lab TDT – 08 L Dissolution testers USP) type 2 (paddle) was used for study. Nine hundred milliliter of phosphate buffer pH 6.8 was taken in vessel and the temperature was maintained at 37 ± 0.5^oC. The speed of the paddle was fixed at 50 rpm. Dissolution samples were withdrawn at two minutes time interval and drug content was determined by measuring the absorbance at 250 nm[11]. Drug concentration was calculated from standard calibration curve and expressed as cumulative percent drug dissolved. *In vitro* dissolution study was also performed similarly on conventional tablet formulation.

Drug-excipient interaction study: The pure drug, mixture of drug with polysaccharide (1:1) and the optimized formulation (Mixture of drug with various excipients used in the preparation of ODT formulation) were characterized by FT-IR spectroscopy to know the compatibility. The scanning range was 500 to 4000 cm^{-1} and the IR spectra of samples were obtained using KBr disc method.

Stability studies: The stability study of the tablets was carried out by keeping the samples in stability chamber at $40^o \pm 20^oc/75\% \pm 5\%$ RH for three months as per the ICH guidelines. The optimized batch was selected for stability studies. Tablets were evaluated for hardness, friability, drug batch content (Assay), disintegration time, in-vitro drug release profile after one month interval.

RESULTS

The polysaccharide isolated from *raw fruits of H. sabdariffa* was a light brown colored powder (Yield = 16.53% w/w). The polysaccharide was soluble in hot water forming colloidal solution and practically insoluble in organic solvents. The pH of 1% w/w solution of polysaccharide was found to be near neutral. Polysaccharide showed good swelling and water absorption capacity. The Carr's index and of repose indicated that the polysaccharide has a good flow with moderate compressibility. The loss on drying and ash values were well within official limits . The results of physicochemical characteristics of polysaccharide are reported in table 2. Drug-excipient interaction studies revealed that there was no physicochemical interaction between Diclofenac sodium and other excipients. All the major peaks of Diclofenac sodium were found in the sample. FTIR analysis of pure drug and optimized formulation (F4) containing diclofenac sodium (D), isolated polysaccharide (HSM) and sodium starch glycolate (SSG) were shown in the Fig. 1, Fig. 2 and Fig. 3 respectively. Weights of all the tablets prepared were within the acceptable limit for uncoated tablets as per Indian Pharmacopoeia. The results of pre-compression parameter evaluation indicated good free flowing properties of the powder blend (Table 3). The hardness of tablets was determined and was found to be in the range of 4.26 to 4.56kg/cm^2. Friability was observed between 0.45% to 0.78% which was less than 1% indicating that tablets had good mechanical resistance. Percentage drug content of all formulations was

Found between 98.48%w/w and 99.40%w/w. The results of post compression parameter are summarized in table 4 and 5. The wetting time and water absorption ratio are important criteria for understanding the capacity of disintegrant to swell in presence of little amount of water. The wetting time for all the formulation was found between 25.95±0.05 and 54.30±0.12 seconds (Table 5). *In vitro* disintegration time for formulations F1 to F8 are is summarized in table 5.

Table 1 Composition of Orodispersible Tablets

Components mg/tablet	Formulation code							
	F1	F2	F3	F4	F5	F6	F7	F8
Drug	50	50	50	50	50	50	50	50
Micro Crystalline Cellulose	141.2	138.2	133.2	128.2	141.2	138.2	133.2	128.2
H.sabdariffa polysaccharide	2	5	10	15	-	-	-	-
Sodium starch glycolate	-	-	-	-	2	5	10	15
Sodium saccharin	2.8	2.8	2.8	2.8	2.8	2.8	2.8	2.8
Vanilla	1	1	1	1	1	1	1	1
Talc	1	1	1	1	1	1	1	1
Magnesium stearate	2	2	2	2	2	2	2	2
Total weight	200	200	200	200	200	200	200	200

Table 2 Physicochemical parameters of isolated polysaccharide

Parameters	Results
State	Solid
Colour	Light brown
p^H	6.93-7
Solubility	Soluble in hot water forming colloidal solution and insoluble in organic solvents
Swelling factor	8 ml
Practical yield	16.53%w/w
Total ash	0.4
Loss on drying	3.6%
Total Polysaccharide content	0
Angle of Repose	22.3^0
Bulk density	0.64 g/cm^3
Tapped density	0.53 g/cm^3
Carr's index	17.16
Hausner's ratio	1.20

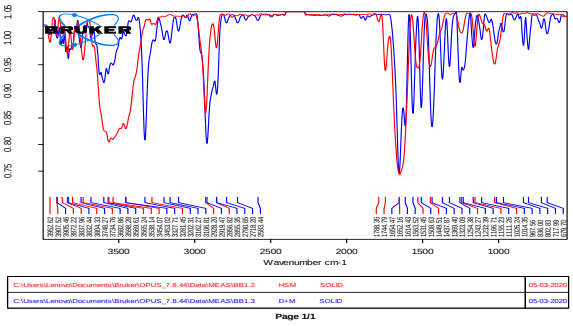

Fig.1. FT-IR Spectrum of Pure Mucilage (HSM) and Optimized formulation and mucilage (D

Formulation code	Parameters				
	Angle of Repose (Ɵ)	Bulk density (g/cm^3)	Tapped density (g/cm^3)	Carr's Index (%)	Hausner's Ratio
F1	29.21±0.50	0.511±0.008	0.641±0.004	21.13±0.66	1.268±0.01
F2	30.24±1.03	0.548±0.01	0.631±0.01	14.24±1.01	1.152±0.04
F3	28.59±0.91	0.517±0.03	0.664±0.004	26.13±0.83	1.347±0.02
F4	28.26±0.21	0.494±0.004	0.645±0.008	21.57±0.34	1.304±0.007
F5	27.74±0.44	0.546±0.005	0.657±0.003	16.21±0.47	1.206±0.02
F6	30.48±0.63	0.523±0.008	0.636±0.005	17.85±0.61	1.216±0.009
F7	28.48±0.47	0.551±0.003	0.628±0.001	12.20±0.50	1.153±0.02
F8	30.59±0.51	0.535±0.02	0.630±0.001	15.41±0.74	1.182±0.01

Table 3- Precompression parameters of powder blend

Formulation code	Parameters			
	Thickness (mm)	Hardness (kg/cm^2)	Fraibility (%)	Weight variation
F1	2.45±0.01	4.56±0.01	0.63±0.04	200.1±0.08
F2	2.35±0.04	4.37±0.01	0.70±0.01	200.0±0.10
F3	2.54±0.01	4.49±0.02	0.75±0.02	200.0±0.02
F4	2.39±0.008	4.26±0.02	0.78±0.02	200.3±0.01
F5	2.28±0.021	4.36±0.02	0.45±0.02	200.0±0.02
F6	2.21±0.02	4.55±0.02	0.56±0.01	200.0±0.01
F7	2.23±0.02	4.48±0.01	0.58±0.004	200.1±0.04
F8	2.27±0.008	4.31±0.01	0.70±0.01	200.3±0.04

Table 4 Post compression parameters of Orodispersible Tablets

Formulation code	Parameters			
	In vitro disintegration time (s)	Wetting time (s)	Water absorption ratio	Drug content
F1	59.90±0.25	46.63±0.02	109.95 ±0.05	99.83±0.08
F2	57.98±0.09	42.72±0.02	120.08±0.04	98.48±0.42
F3	47.32±0.39	37.24±0.07	125.95±0.04	99.58±0.42
F4	32.16±0.04	25.95±0.05	134.02±0.05	99.90±0.04
F5	69.22±0.02	54.30±0.12	99.81±0.04	98.48±0.10
F6	61.76±0.04	50.56±0.09	99.17±0.05	98.84±0.04
F7	55.06±0.07	47.78±0.08	103.96±0.04	99.83±0.05
F8	33.11±0.12	39.38±0.08	139.94±0.06	99.93±0.04

Table 5 Post compression parameters of Orodispersible Tablets

Parameters	1st Month	2nd Month	3rd Month
Hardness (kg/cm2)	4.38±0.09	4.22±0.1	4.41±0.12
% Friability	0.76±0.09	0.79±0.03	0.77±0.05
Drug content (%)	99.53±0.45	99.83±0.1	99.95±0.19
Disintegration time(sec)	32.84±0.6	31.72±0.9	33.28±0.1

Table 6 Stability study data for F4 batch

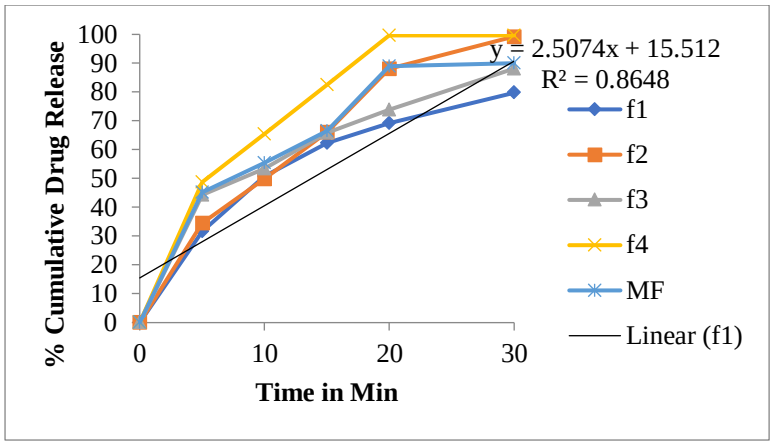

Fig.2. *In vitro* drug release profile of formulations (F1-F4and marketed formulation)

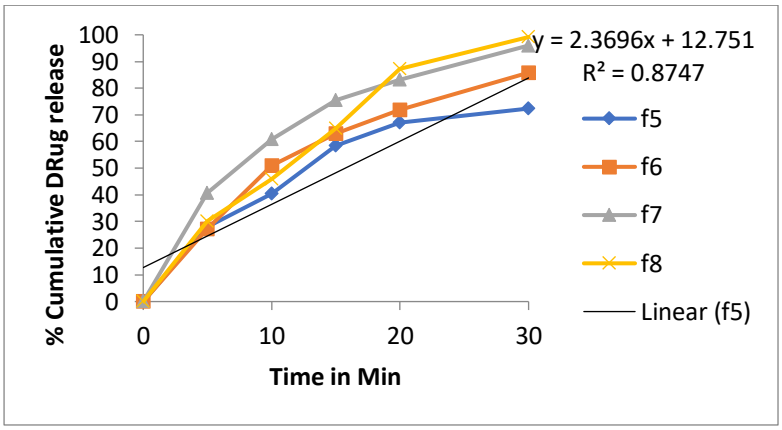

Fig.3. *In vitro* drug release profile of formulations (F5-F8)

In vitro drug release rate from the formulations containing polysaccharide was found to be rapid as compared to the formulations containing sodium starch glycolate. The *in vitro* drug release profiles of formulations F1 to F8 are represented in fig 2 and 3. The results of stability study indicated that there was no significant change on physical and chemical characteristics of the tablet and the optimized formulation F4 containing 7.5% of polysaccharide was stable at 40^{o}C/75% RH for 3 month (Table 6)

DISCUSSION

It was reported that raw fruits of *H. sabdariffa* are mucilaginous. Many fruit mucilages have been used as superdisintegrant. Hence on similar basis *H. sabdariffa* mucilage has been studied for its superdisintegrant property. It was observed that *H. sabdariffa* has good swelling properties. Therefore we have attempted to develop orodispersible tablets from polysaccharide isolated from seeds of *H. sabdariffa* in order to investigate its potential as a superdisintegrant. There are various reported mechanisms of superdisintegrants like swelling, wicking, deformation and electrostatic repulsion. Orodispersible tablets of Diclofenac sodium were prepared by direct compression method using different concentrations *H. sabdariffa* mucilage as a natural disintegrant and sodium starch glycolate as synthetic superdisintegrant in the same concentration. The excipients were selected depending upon preformulation studies and their concentrations were established on the basis of extensive literature survey. Microcrystalline cellulose was selected as a directly compressible diluent. Sodium saccharin was selected as a sweetening agent and vanilla was used as flavour. Since direct compression method was used for preparation of tablets, Magnesium stearate was chosen as lubricant to improve flow properties of the blend. Tablets prepared using polysaccharide isolated from *H. sabdariffa* took lesser time for

wetting of tablet as compared to the formulations containing sodium starch glycolate. This might be due to rapid penetration of water into the pores of tablets. Water absorption ratio of polysaccharide was higher as compared so that of sodium starch glycolate. It was observed the water absorption ratio increased with an increase in concentration of superdisintegrant. Because of higher swelling property, formulations containing polysaccharide disintegrated quickly and completely as compared to formulations containing sodium starch glycolate. Rapid increase in dissolution of drug with increase in polysaccharide content may be attributed to swelling of polysaccharide powder which leads to penetration of water into the pores of tablets and generation of hydrodynamic pressure for quick and complete disintegration of tablets. However incase of tablet prepared by sodium starch glycolate, disintegration takes place by rapid uptake of water followed by quick and enormous swelling into smaller particles but dissolution occurs slowly due to formation of viscous gel layer by sodium starch glycolate. The drug release of F4 formulation was rapid and better than marketed formulation. The formulation F4 containing 7.5% of polysaccharide showed rapid wetting time and disintegration time as compared to formulation prepared using synthetic superdisintegrant at the same concentration level. Hence batch F4 was considered as optimized formulation.

CONCLUSION

The present work revealed that the polysaccharide isolated from the raw fruits of *Hibiscus sabdariffa* L can be a potent natural super disintegrant based on the results obtained. *H. sabdariffa* polysaccharide is inexpensive as compared to synthetic superdisintegrant, non-toxic, compatible and easy to manufacture, it can be used in place of commercially available synthetic superdisintegrants. The prepared tablets also gives advantage in terms of patient compliance, quick onset of action, high bio-availability and good stability which make these tablets as a better dosage form. However low percentage yield and moderate swelling properties are the disadvantages we observed in this study. Hence future work must be undertaken to improve the percentage yield and studies must be conducted to prove the impact of swelling on disintegration. The advantage of *Hibiscus sabdariffa* L polysaccharide is its edible nature hence it is a suitable candidate for use in oral drug delivery applications where the toxicity-related regulatory issues can be easily addressed.

REFERENCES

1. Radha Rani Earle, Lakshmi Usha Ayalasomayajula, A. Naga Raju, K. Tanuja Kumari and P. Ravi Kumar, Formulation and evaluation of diclofenac sodium oro dispersible tablets using different superdisintegrants by direct compression technique, Der Pharmacia Lettre, 2016, 8 (8):227-238
2. Swamy NGN, Sachin, Abbas Z, Journal of Applied Pharmaceutical Science, 2012, 2, 11, 40-49.
3. Harshal Pawar, Chhaya Varkhade, Pravin Jadhav, Kavita Mehra, Development and evaluation of orodispersible tablets using a natural polysaccharide isolated from *Cassia tora* seeds.Integrative Medicine Research, 3(2), 2014, 91-98.
4. Erumalla Venkatanagaraju, N. Bharathi, Rachiraju Hema Sindhuja, Rajshree Roy Chowdhury and Yarram Sreelekha (April 10th 2019). Extraction and Purification of Pectin from Agro-Industrial Wastes, Pectins - Extraction, Purification, Characterization and Applications, Martin Masuelli, IntechOpen, DOI: 10.5772/intechopen.85585.
5. Inês Da-Costa-Rocha, Bernd Bonnlaender, Hartwig Sievers, Ivo Pischel, Michael Heinrich, *Hibiscus sabdariffa* L. – A phytochemical and pharmacological review, Food Chemistry, 165, 2014, 424-443.
6. KR Khandelwal (2008). Practical pharmacognosy techniques and experiments, Nirali Prakashan . 159.
7. Indian Pharmacopoeia. (1996) Controller of publications. 4th ed. Ministry of Health and Family Welfare, Govt. of India. New Delhi, India. 1:78.

8. Leon L, Herbert AL, Joseph LK. The theory and practices of industrial pharmacy.3rd ed. Varghese publishing house 2008; 296-303, 430-456.
9. Zhao N, Augsburger LL. Functionality comparison of three classes of super-disintegrants in promoting aspirin tablets disintegration and dissolution. AAPS Pharm Sci Tech 2005; 6: 634-40.
10. Chaudhari PD, Chaudhari SP, Kohle SR, et al. Formulation and evaluation of fast dissolving tablets of famotidine. Indian Drug 2005; 42: 641-649.
11. Rangole US, Kawtikwar PS, Sakarkar DM. Formulation and *in vitro* evaluation of rapidly disintegrating tablets using hydrochlorothiazide as a model drug. Res J Pharm Tech 2008; 1: 349-352.