Available online www.jocpr.com

Journal of Chemical and Pharmaceutical Research, 2014, 6(10):155-159

Research Article

ISSN : 0975-7384
CODEN(USA) : JCPRC5

Evaluation of *Terminalia randii* Baker F. gum as a disintegrant in paracetamol tablet formulation

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ABSTRACT

This study aims at evaluating the disintegrant properties of Terminalia randii gum at various concentrations in Paracetamol tablet formulation in comparison with a standard disintegrant (corn starch) using wet granulation method. The mechanical properties of the tablets were assessed using crushing strength and friability while the release properties were assessed using the disintegration and dissolution times. Data were analysed using ANOVA. The crushing strength of formulations containing corn starch was observed to decrease with increase in disintegrant concentration, while those containing terminalia gums was observed to increase with increase in concentration. Formulations containing Terminalia randii gum generally had lower mechanical strength at lower concentrations and significantly ($P<0.001$) higher disintegration times than those containing corn starch. The disintegration time was observed to be within fifteen (15) minutes specified for uncoated tablets. The time taken for 50% dissolution (T_{50}) of formulations containing corn starch was significantly ($P<0.05$) lower than that of formulations containing terminalia gum but there was no significant difference in the T_{90} of the formulations. The results show that Terminalia randii gum compared favourably with official corn starch and it could serve as an alternative disintegrant in tablet formulations.

Key words: *Terminalia randii* gum, disintegrant, mechanical strength, disintegration times, dissolution times

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INTRODUCTION

Disintegrants are excipients added to tablet and some encapsulated formulations to promote the breakup of the tablet and capsule into smaller fragments in an aqueous environment there by increasing the available surface area and thus promoting a more rapid release of the drug substance [1]. The solubility of a drug in the gastrointestinal fluid and its permeability across the gastrointestinal membrane affects the absorption and bioavailability of the drug. The drug's solubility depends mainly on its physicochemical properties. However, disintegration is the rate limiting step in drug dissolution. The drug will dissolve at a slower rate from a tablet without a disintegrant. Disintegrants can be added intragranular, extragranular and partly intragranular and extragranular. Disintegrants that have been used in pharmaceutical formulations includes starch [2], cellulose, mucilages and gums [3,4]. The rate of dissolution of a drug substance in many solid dosage forms is the rate determining step for absorption which would subsequently lead to therapeutic efficacy of the drug. However, in most formulations, disintegration precedes drug dissolution. Hence, the need to choose a disintegrant with predictable and consistent performance when formulating tablets [5].

Recent studies have shown the potentials of terminalia gum obtained from the incised trunk of *Terminalia randii* (Combretaceae) as a binding agent in carvedilol tablet formulations [6] and as a directly compressible excipient for controlled drug delivery [7]. In this present work, gum obtained from the incised trunk of *Terminalia randii* (Combretaceae) has been evaluated as a disintegrant in paracetamol formulations in comparison with corn starch.

EXPERIMENTAL SECTION

Materials and Methods

The materials used were paracetamol powder BP, corn starch (BDH chemicals, UK) polyvinylpyrrolidone USP K29/32 (molecular weight:58,000) (ISP Technologies, Inc Wayne, USA), magnesium stearate (Loba Chemie Pvt Ltd, Mumbai, India), Talc (Loba Chemie Pvt Ltd, Mumbai, India) and terminalia gum obtained from *Terminalia randii (Family* Combretaceae) was collected from Olabisi Onabanjo University Ago-Iwoye. A description of the collection and purification of the gum has been given elsewhere[6].

Determination of swelling index

10g of the disintegrants were weighed into a 100 mL measuring cylinder. The volumes occupied by the disintegrants were noted (V_1). Distilled water was added and the mixture was shaken. Distilled water was added and made up to 100 ml. The cylinder was allowed to stand for 24 hours and the final volume was noted (V_2). The swelling index was then calculated from the ratio of the volume occupied by the powder after swelling to the initial volume occupied by the powder after adding water. The test was performed in triplicate and the swelling capacity calculated from the mean of the three tests.

Preparation of granules

100g of paracetamol was weighed into a planetary mixer (Model A120, Hobart Manufacturing Co, U.K) and moistened with aqueous solution of polyvinylpyrollidone (5%w/v). Massing was continued for 5 minutes and the wet masses were granulated by passing them manually through a number 12 mesh sieve (1400 µm), dried in a hot air oven for 4 hours at 60 ^{o}C and then re-sieved through a number 16 mesh sieve (1000 µm) and then stored in air tight container. Disintegrants (Terminalia randii gun, Corn starch) were added extragranularly to the granules at different concentrations (1-10%w/w).

Determination of granule properties

The angle of repose of granules was determined by the fixed funnel method [8]. The bulk and tapped densities were determined by weighing 2 g (W) of granule a 10 mL measuring cylinder. After the initial volume (V_O) was measured and the cylinder was tapped on a hard surface until no further change in volume was observed. The tapped volume (V_T) was noted. Bulk density (BD) and tapped density (TD) were calculated using the following formula:

$$BD = W / V_O$$

$$TD = W / V_T$$

Preparation of tablets

500 mg of paracetamol granules was compressed for 30 seconds into tablets with predetermined loads on a Carver hydraulic press (Model C, Carver Inc. Wisconsin, USA), using a 10.5 mm die and flat faced punches lubricated with a 1 % dispersion of magnesium stearate in acetone prior to compression. After ejection, the tablets were stored over silica gel for 24 hour to allow for elastic recovery and hardening.

Evaluation of tablet properties

20 tablets were selected randomly from each batch and weighed individually using a top-loading electronic balance. The average weight was noted and standard deviation calculated. Friability was determined using a friability test apparatus (Veego Scientific devices, Mumbai, Maharashtra, India) at 25rpm for 4 minutes. Determination was in quadruplicate. Crushing strength was determined using a Mosanto hardness tester (Mosanto, Cambridge, UK). Determination was in quadruplicate. Disintegration time was carried out in distilled water at 37±0.5^{o}C on a disintegration test apparatus (Manesty Machines, Poole, UK). Determination was in quadruplicate. *In vitro* dissolution was carried out in 900mL phosphate buffer (pH 5.9) at a constant temperature of 37±0.5^{o}C using a USP Type 2 dissolution apparatus (Labindia Dissolution test apparatus DISSO 2000, Labindia instruments PVT Ltd, Thane, India) rotated at 100rpm. Samples (5mL) were withdrawn at different time intervals and replaced with fresh

medium. The samples were diluted and the amount of paracetamol released was determined using a UV spectrophotometer at a wavelength of 243nm. Determination was in quadruplicate.

Statistical analysis

Statistical analysis was done to compare the effect of the different binders on the tablet properties using ANOVA (GraphPad Software Incorporation, San Diego, USA). At 95% confidence interval, p values of ≤ 0.05 were considered significant.

RESULTS AND DISCUSSION

The flow property of a powder is essential in determining its suitability as direct compression excipients. The flowability is of immense importance in all volume filling of powders as in production of tablets and capsule. The angle of repose is considered as indirect measurement of powder flowability. Table 1 show that the value of the angle of repose was found to be 19.50^0-26.93^0 indicating good flow properties. The swelling capacity has been shown to have significant effect on their disintegrating properties as it is well known that one of the mechanisms of action of disintegrants is swelling [2]. The swelling index of terminalia is higher than that of corn starch. The properties of the granules prepared were determined before compression. There were no significant ($p>0.05$) differences in the granule properties of granules containing terminalia gum and starch as disintegrants. The tablet properties of formulations containing *Terminalia randii* and cornstarch are presented in Table 2. There was no significant ($p>0.05$) difference in the weight of the tablets due to the good flow properties of the granules [9].

The mechanical strength of a tablet provides a measure of the bonding potential of the material concerned and this information is useful in the selection of excipients. An excessively strong bond may prevent rapid disintegration and subsequent dissolution of a drug. Weak bonding characteristics may limit the selection and/or proportion of excipients, such as lubricants, that would be added to the formulation. The mechanical properties of the tablets were assessed using crushing strength and friability. Crushing strength of formulations containing corn starch decreased with increase in concentration of the disintegrant, while formulations containing terminalia gum increased with increase

Table 1: .Precompression parameters data for Paracetamol granules

Type of disintegrant	Concentration of disintegrant (%)	Bulk density (g/mL)	Tapped density (g/mL)	Angle of repose (^{0})
Corn starch	1.00	0.38	0.50	23.73
	2.00	0.42	0.50	19.50
	5.00	0.42	0.45	22.03
	7.50	0.42	0.45	24.30
	10.00	0.45	0.45	26.00
Terminaliagum	1.00	0.42	0.45	24.77
	2.00	0.42	0.45	22.83
	5.00	0.42	0.42	25.37
	7.50	0.42	0.42	24.44
	10.00	0.42	0.42	26.93

in concentration of disintegrant. The friability values of formulations containing terminalia gum decreased with increase in concentration of the disintegrants. The crushing strength-friability ratio (CSFR) also provides a parameter for measuring tablet strength [7, 10]. The higher the CSFR value, the stronger the tablet is generally. The values of CSFR for all formulations are included in Table 2. An increase in CSFR was observed for the tablets with increase in disintegrant concentration, highlighting the dual role of the polymers within the formulations.

The disintegration time was observed to decrease with increase in concentration of the disintegrants (Fig 1). All the formulations passed the disintegration time test, i.e. uncoated tablets should disintegrate within 15 minutes [11].The disintegration time of formulations containing terminalia gum was between 0.7-2.62 minutes. It would have been expected that formulation containing terminalia gum would have lower disintegration time due to the high swelling index. The higher disintegration time could have been due to the fact that when gums come in contact with water, they swell, forming a film which led

Table 2: Tablet properties

Type of disintegrant	Concentration of disintegrant (%)	Weight (g)	Friability (%)	Crushing strength (N)	CSFR	Disintegration time (minutes)	CSFR/Dt	t_{50} (Minutes)	t_{80} (Minutes)
	0	489±2.85	1.91±0.50	6.72±0.76	3.52	>20minutes		>60	>60
Corn starch	1.00	489±3.27	1.44±0.02	12.74±0.28	8.85	0.37±0.11	23.9	<1	13.50±0.32
	2.00	488±2.69	1.51±0.14	11.37±0.45	7.53	0.18±0.04	41.8	<1	14.00±0.43
	5.00	488±2.12	1.34±0.52	11.25±0.45	8.40	0.17±0.03	49.4	<1	9.00±0.24
	7.50	488±3.41	1.39±0.04	10.92±0.12	7.86	0.12±0.07	65.5	<1	8.00±0.31
	10.00	488±3.46	1.69±0.27	10.09±0.27	5.97	0.08±0.04	74.6	6.00±0.21	53.00±0.93
Terminalia gum	1.00	491±3.81	2.09±0.65	8.57±0.76	4.10	2.62±0.37	1.6	27.00±0.52	49.00±0,87
	2.00	490±2.68	1.72±0.47	9.88±0.45	5.74	0.83±0.23	6.9	8.50±0.09	19.50±0.13
	5.00	489±3.20	1.36±0.09	10.81±0.79	7.95	0.75±0.03	10.6	9.00±0.14	23.00±0.26
	7.50	487±3.99	1.02±0.13	10.82±0.92	10.61	0.73±0.15	14.5	8.00±0.36	18.00±0.62
	10.00	487±2.71	0.86±0.25	10.90±0.13	12.67	0.70±0.02	18.1	8.00±0.23	22.00±0.74

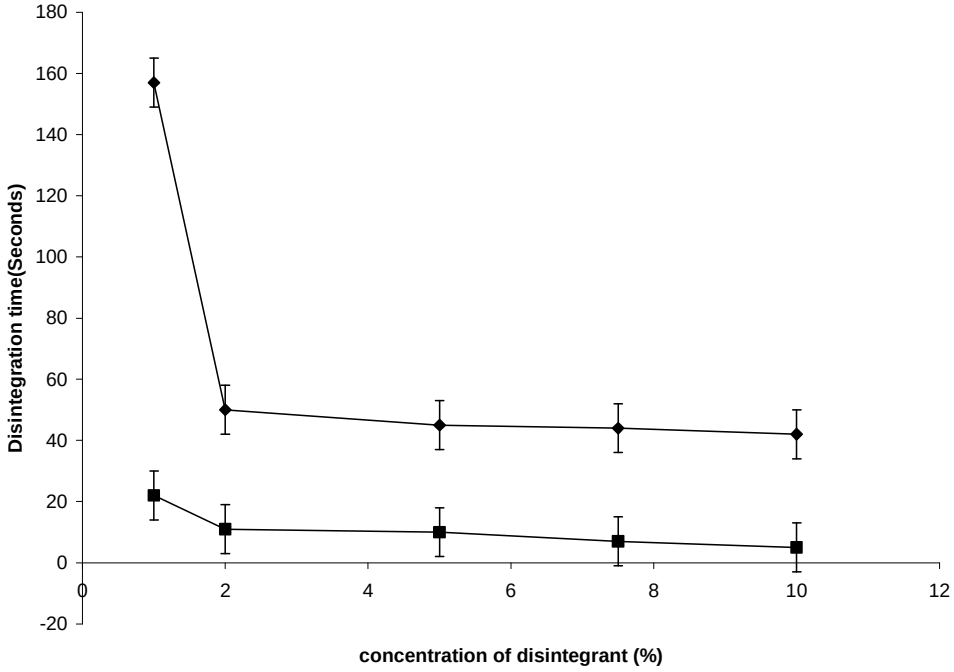

Figure 1. Plot of disintegration time of paracetamol tablet formulations against concentration of disintegrants ■Corn starch, ◆Terminalia gum

to the reduction in penetration of water into the tablet, thus increasing the disintegration time of the tablet. Further, the crushing strength-friability/disintegration time ratio (CSFR/D) has been shown to be a more relevant index because in addition to measuring net tablet strength, it simultaneously relates the ratio of this parameter to disintegration [12]. The value of CSFR/D serves to evaluate any negative influence of net tablet strength on disintegration time. Generally, higher values of CSFR/D indicate stronger tablets with a better balance between binding and disintegration properties. The CSFR/D values for the different formulations are presented in Table 2.

The representative plot of percentage drug released against time of paracetamol formulations containing disintegrant at 10% w/w concentration is shown in Figure 2. It was observed that formulations without disintegrant has the lowest percentage of drug released. This shows the importance of disintegrant in formulations. The dissolution time was assessed using t_{50} and t_{90} (time taken for 50% and 90% of the drug to be released respectively). The t_{50} of

formulations containing corn starch was significantly ($p<0.05$) lower than that of formulations containing terminalia gum. There was no significant difference in the t_{90} of the formulations except at 10% w/w at which formulations containing terminalia gum gave significantly ($p<0.05$) lower dissolution time.

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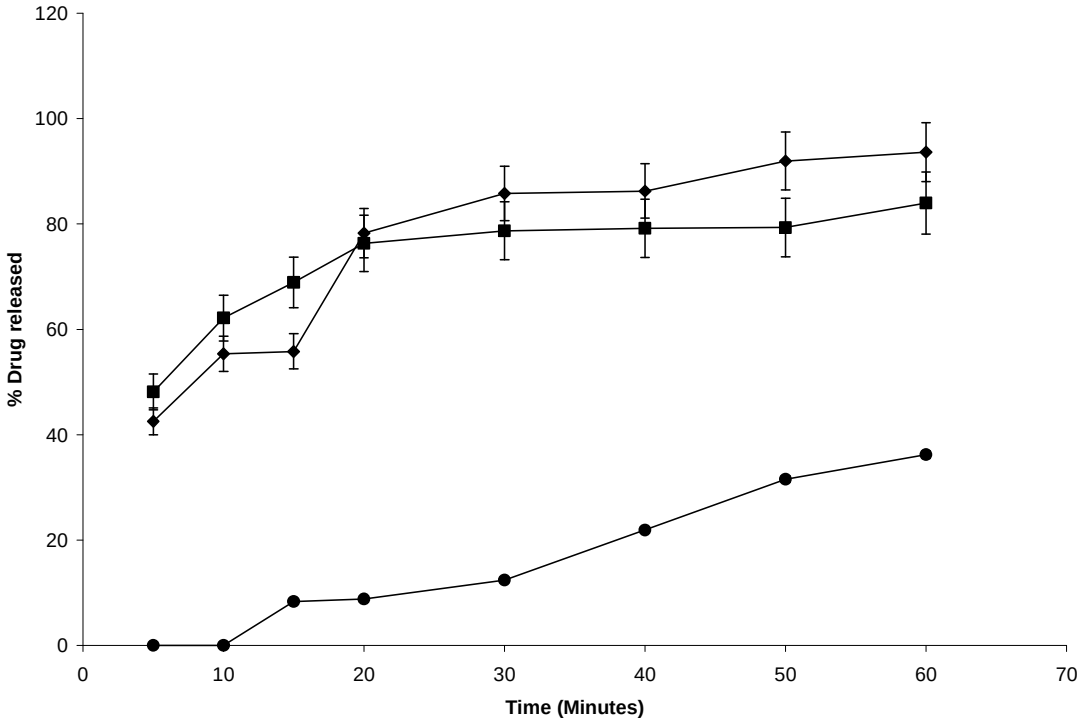

Figure 2. Representative plot of percentage drug released from paracetamol tablets Containing 10% w/w disintegrant ■ Corn starch, ◆ terminalia gum, ● 0%w/wdisintegrant

CONCLUSION

Terminalia randii gum compared favorably well with cornstarch as a disintegrant in tablet formulations and it could be used as an alternative disintegrant in drug formulations

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