

## FORMULATION AND EVALUATION OF METRONIDAZOLE TABLETS USING NATURAL GUM

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## ABSTRACT

**Objectives:** The objective of the present study was to formulate the metronidazole tablets using natural *Aloe vera* gum as binding agent.

**Materials and Methods:** To determine the binding properties of the extracted *A. vera* gum were used for the preparation of metronidazole tablets and compared with other binding agents such as acacia and sodium carboxymethyl cellulose (CMC). Physical properties such as hardness, friability, disintegration time, and *in vitro* dissolution rate are the important parameter which determines for each formulation. Three batches of metronidazole tablets are prepared using acacia (F1), sodium CMC (F2), and *A. vera* gum (F3) as binding agent.

**Results:** The granules were evaluated by determining the angle of repose ( $26.01 \pm 0.110$ – $27.18 \pm 0.166^\circ$ ), bulk density, tapped density, Hausner ratio, and Carr's index. It shows satisfactory results. At time 90 min, the percentage release of drug for F1, F2, and F3 was 44.947%, 31.467%, and 53.424%, respectively. The tablets prepared with *A. vera* gum showed faster release profile than other binders.

**Conclusion:** From the results, it was shown that tablets prepared with *A. vera* gum have good binding properties and also helped tablets for faster release.

**Keywords:** *Aloe vera*, Metronidazole, Binder.

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## INTRODUCTION

Dosage forms usually consist of several materials, in addition to the drug that they convey to the patient. These materials are generally referred to as tablet excipients. An excipient can be defined as any component, other than the active substances, intentionally added to the formulation of a dosage form for the purpose of long-term stabilization and to increase therapeutic enhancement in the final dosage form, such as drug absorption and reducing viscosity [1]. In tablets, the excipients frequently added include diluents, binding agents, disintegrants, lubricants, and glidants [2].

Binders are pharmaceutical excipients that are commonly used in tablet formulations to mix the powders properly and form proper granules and hence generally improve the flow properties of the granules [3, 4]. They modify the binding properties of the granules by promoting the formation of strong cohesive bonds between particles [5]. They have been used as solutions and in dry forms depending on other ingredients in the formulation and the method of preparation [6]. Gums are mainly long chain, straight or branched chain polysaccharides that contain hydroxyl groups that bond to water molecules [7]. A number of plant gums/hydrocolloids have been used as binding agents, suspending or emulsifying agents in both solid and liquid dosage forms [8, 9].

These gums are generally non-toxic and widely available hence the continued interest [10]. Aloe gum is the yellow juice exudates produced from most aloe varieties. The bulk of research done on aloe has been on its medicinal properties and it has many of such properties. Its medicinal properties include wound healing, purgative, immunostimulation, anti-inflammatory, and promotion of radiation damage repair [11]. The primary components of aloe are aloin, barbaloin, isobarbaloin, aloe-emodin, and resins. It also contains aloetic acid, galacturonic acid, glucosamine, monosaccharides, and polysaccharides.

There is a prevailing need to develop cheaper and easily accessible tablet excipients, especially in developing countries to reduce the cost of

production of tablets. The basis of this research is, therefore, to explore the possibility of using *Aloe vera* gum as a tablet excipient since it is easily cultivatable and readily available. Therefore, our main objectives of the present study were to formulate the metronidazole tablets using natural *A. vera* gum as binding agent and compare with other binders.

## MATERIALS AND METHODS

## Chemicals and reagents

Metronidazole powder (Yellow Chem Pvt. Ltd.), acacia (Loba Chemie), sodium carboxymethyl cellulose (CMC) (Loba Chemie), magnesium stearate (Loba Chemie), microcrystalline cellulose (Merck Ltd.), lactose (Merck Ltd.), talc (Loba Chemie), HCl (International Chemicals, India), and ethanol (Changshu Hongsheng Fine Chemicals Co. Ltd.) were used.

## Preparation of metronidazole tablets

Three batches of the metronidazole tablets were formulated using three binders, namely acacia, sodium CMC, and *A. vera* gum. Wet granulation method was used in the formulation of the tablets. Metronidazole powder was triturated together with other ingredients (microcrystalline cellulose and lactose) in geometric order using mortar and pestle. Weighed quantity of each binder was mixed with 8 ml of water to form mucilage and then, used to form a damp mass with the powder mix. The damp mass was passed through 1.7 mm sieve and dried in a hot oven. The resultant dried granules were passed through 1.0 mm sieve and then through 0.25 mm sieve to separate the fine from coarse granules. Magnesium stearate was mixed with the fines and coarse granules then added and all mixed together. The granules mixture was compressed into tablets using a single punch machine [12].

## Characterization of granules flow characteristics

## Bulk density

The bulk density of a material is the ratio of the mass to the volume (including the interparticulate void volume) of an untapped powder sample. The bulk density is obtained by adding known mass of powder

to a measuring cylinder. The density is calculated as mass/volume. The bulk density is given in g/ml [13].

Bulk density = Mass of the powder/Bulk volume

#### Tapped density

The tapped density is obtained by mechanically tapping a graduated cylinder containing the sample until little further volume change is observed. The tapped density is obtained by mechanically tapping a graduated cylinder containing the sample until little further volume change is observed. The tapping can be performed using different methods. The tapped density is calculated as mass divided by the final volume of the powder [13,14].

Tapped density = Mass of the powder/Tapped volume

#### Compressibility index or Carr's index and Hausner ratio

The compressibility index and Hausner ratio are measured of the products ability to settle and permit an assessment of the relative importance of interparticulate interactions. In a free-flowing powder, these interactions are less significant and the bulk and tapped densities will be closer in value. For poorly flowing materials, there are greater interparticulate interactions and a greater difference between the bulk and tapped densities will be observed. The differences are reflected in the compressibility index and Hausner ratio [13,14].

Compressibility index = (Tapped density - Bulk density)/Tapped density × 100

Hausner ratio = Tapped density/bulk density

#### Angle of repose

This is the maximum angle possible between the surface of a pile of powder or granules and the horizontal plane [14].

$$\text{Angle of repose} = \tan \theta = h/r$$

$$\theta = \tan^{-1} (h/r)$$

Where,  $\theta$  = angle of repose, h = height of the heap, and r = radius of the heap

#### Evaluation test of metronidazole tablets

##### Hardness test

Hardness of tablets was measured by Monsanto hardness tester [15].

##### Friability Test

The friability of the tablets was measured by Roche friabilator [16].

##### Disintegration time

The disintegration time is measured by the USP disintegration apparatus [16].

##### Dissolution studies

Dissolution rate test was performed with an apparatus meeting the requirement of the United States Pharmacopoeia. The dissolution apparatus (Electrolab) Type II operated at 50 rpm was used. The dissolution medium consisted of 900 ml of freshly prepared 0.1 N HCl contained in a 1 l beaker. The temperature was maintained at  $37 \pm 0.5^\circ\text{C}$ . Adequate dilutions of the withdrawn samples were made and the absorbance was measured at 278 nm using the array spectrophotometer (ELICO) [16].

## RESULTS AND DISCUSSION

Natural binders are considered to be very useful constituents for the development of different tablet preparation as safe with less or no side

effect. *A. vera* gum shows good binding properties with comparison to acacia and sodium CMC [17].

The bulk density of all three batches F1, F2, and F3 was  $0.3547 \pm 0.006$  g/ml,  $0.3220 \pm 0.004$  g/ml, and  $0.3179 \pm 0.003$  g/ml, respectively. The tapped densities were  $0.4235 \pm 0.006$  g/ml,  $0.3765 \pm 0.007$  g/ml, and  $0.3843 \pm 0.002$  g/ml, respectively. The Carr's index values were  $0.1624 \pm 0.012\%$ ,  $0.1442 \pm 0.022\%$ , and  $0.1732 \pm 0.008\%$ , respectively. Hausner ratio values were  $1.1944 \pm 0.017$ ,  $1.1700 \pm 0.030$ , and  $1.2105 \pm 0.017$ , respectively. The angles of repose were  $26.01 \pm 0.110$ ,  $26.36 \pm 0.678$ , and  $27.18 \pm 0.166$ , respectively. All the results were shown in Table 1. It also showed satisfactory results.

The result of hardness test of three batches F1, F2, and F3 was  $3.90 \pm 0.82$ ,  $3.75 \pm 0.63$ , and  $4.10 \pm 0.58$ , respectively. The hardness of tablet prepared was acceptable within 4–7 kg/cm<sup>2</sup>. If the concentration of the binder increases, the hardness can also be increase and the type of binder change also leads to an increase in hardness value. This may be occurred due to the more solid bond between particles and the concentration of binder increases the hardness value [18].

The percentage friability of F1, F2, and F3 batches was  $0.77 \pm 0.010$ ,  $0.57 \pm 0.003$ , and  $0.63 \pm 0.001$ , respectively. The results of friability of

Table 1: Pre-compression parameter of granules

S.No	Properties	F1 (acacia as binding agent)	F2 (sodium CMC as binding agent)	F3 ( <i>Aloe vera</i> as binding agent)
1	Bulk density (g/ml)	0.3547±0.006	0.3220±0.004	0.3179±0.003
2	Tapped density (g/ml)	0.4235±0.006	0.3765±0.007	0.3843±0.002
3	Carr's index (%)	0.1624±0.012	0.1442±0.022	0.1732±0.008
4	Hausner ratio	1.1944±0.017	1.1700±0.030	1.2105±0.017
5	Angle of repose	26.01±0.110	26.36±0.678	27.18±0.166

\*All values are express as mean±(t×SEM), n=3. SEM: Standard error of mean, CMC: Carboxymethylcellulose

Table 2: Post-compression result

S.No	Properties	F1	F2	F3
1	Hardness (kg/cm <sup>2</sup> )	3.90±0.82	3.75±0.63	4.10±0.58
2	Friability (%)	0.77±0.010	0.57±0.003	0.63±0.001
3	Disintegration time (min)	22±0.11	18.37±0.25	14.23±0.23

\*All values are express as mean±(t×SEM), n=6. SEM: Standard error of mean

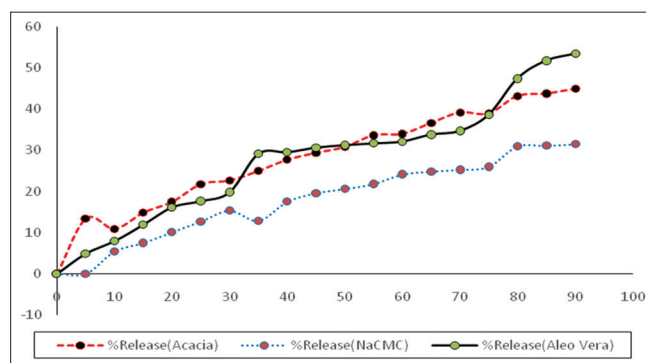


Fig. 1: Percentage release curve of metronidazole tablets using acacia, sodium CMC, and *Aloe vera* as binding agent

all batches were within acceptable value. The percentage friability is the reflection of crushing strength [19]. The results are shown in Table 2.

The disintegration times of three batches were  $22 \pm 0.11$  min,  $18.37 \pm 0.25$  min, and  $14.23 \pm 0.23$  min, respectively. Formation of additional solid bonds that will result in a reduction in the size of the capillary spaces between the particles which reduced the rate of water penetration into the tablets to effect swellability and thus an increase in the disintegration time [20].

In general, the relationship between the binder concentration and percentage of drug release is inverse proportional to each other. If the binder concentration increases, then as a results in the formation of more solid bonds in the tablets which leads to increased tensile strength of the tablets and hence a reduction in disintegration and dissolution rates [21]. The percentage release of drug is shown in Fig. 1 for different binder. At time 90 min, the percentage release of drug for acacia, sodium CMC, and *A. vera* was 44.947%, 31.467%, and 53.424%, respectively. In graph, it was seen that the percentage release of tablet with binder *A. vera* is increase with time than acacia and sodium CMC. The aloe gum tablet is faster release, whereas the sodium CMC tablet is much slower may be due to its polymeric in nature.

### CONCLUSION

Release study of metronidazole tablets using *A. vera* gum was better than acacia and sodium CMC. However, long-term stability study is required for future development of these formulations.

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### AUTHORS' CONTRIBUTIONS

Each author is equally contributed.

### CONFLICTS OF INTEREST STATEMENT

There are no conflicts of interest.

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