Formulation and Evaluation of Floating Matrix Tablets of Ciprofloxacin Using *Sida acuta* Gum

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**Abstract**

**Background:** Natural polymers have been found to be affordable, easily available, biocompatible and biodegradable. This study was conducted to formulate and evaluate floating matrix tablets of ciprofloxacin using *Sida acuta* gum (SAG) as hydrophilic polymer.

**Methods:** *Sida acuta* gum was isolated from the dried powdered leaves of *Sida acuta* plant by isopropyl alcohol precipitation of the filtrate obtained from its maceration in distilled water. The gum obtained was used to formulate ciprofloxacin floating tablets using direct compression technique. The tablets were evaluated for hardness, friability, uniformity of content, floating lag time, total buoyancy time, *in vitro* drug release, kinetics and mechanism of release.

**Results:** The formulated tablets gave hardness range of 3.80 ± 0.56 to 5.01 ± 0.61; uniformity of content value range from 99 to 106%, friability values obtained from 0.44 to 2.41%, and formulated tablets had buoyancy time greater than 12 hours, floating lag time values ranged from <1 min to 90 min. Tablets formulated with 20% hydroxypropylmethylcellulose, HPMC (CF4) gave the highest swelling value of almost 5000%. The drug release profile for the floating tablet formulations after 7 h was 110%, 72%, 106%, 46% and 87% for CF1 (20% SAG), CF2 (30% SAG), CF3 (15/15% SAG and HPMC), CF4 (20% HPMC), CF5 (20% Sodium carboxymethylcellulose) respectively.

**Conclusion:** This study showed that ciprofloxacin floating matrix tablets that have sustained release property could be formulated using *Sida acuta* gum as the hydrophilic polymer.

**Keywords:** Ciprofloxacin; Floating tablets; *Sida acuta* gum; Matrix tablets; Sustained release property

**Introduction**

Most drugs are usually administered through the oral route because it is easier to do so compare to other routes and this leads to better patient compliance. Formulation of oral drugs is usually simple and flexible. Oral dosage forms have a draw back in that due to the variability in gastric emptying time, some may be ejected from the gastric region before the drug is released from the dosage form. This draw back can be resolved by designing drugs that are retained in the gastric region for a long period. This could result in increased bioavailability, decrease in drug waste and enhance the solubility of a drug that is less soluble at high pH concentration [1,2].

Floating or low density system is one of the mechanisms used in the formulation of gastro-retentive dosage forms [3]. In floating systems; the drug is released slowly as it floats on the gastric contents, after which, the residual system is eliminated from the stomach and this leads to extended gastric retention time as well as better control of the variations in plasma drug concentration [4].

Floating systems could be either the effervescent or non-effervescent type. Effervescent systems are matrix type systems. They are produced by compressing a mixture of polymer that swells (e.g., sodium carboxymethylcellulose) and effervescent components like sodium bicarbonate, calcium carbonate, citric acid or tartaric acid. They give out carbon dioxide when they come in contact with gastric juice in the stomach. The carbon dioxide released is trapped in the swollen hydrocolloids and provides buoyancy to the dosage form.

Drugs that are good candidates for formulation into floating drug delivery systems include drugs which have site-specific absorption in the stomach or upper parts of the small intestine (chloridiazepoxide); drugs that exert local therapeutic action in the stomach (antacids), drugs that degrade in the lower part of gastrointestinal tract (metronidazole), drugs that are insoluble in intestinal fluids (diacepam), drugs that disturb the normal colonic bacteria (amoxicillin trihydrate) [1,2].

Ciprofloxacin hydrochloride is an antibacterial agent which is absorbed mainly from the stomach and the proximal part of the small intestine [5]. It is a fluoroquinolone and is active against both gram negative and positive bacteria. Its oral bioavailability is 70% and a peak plasma concentration of 2.5 µg/ml is reached in 1 to 2 h after administration of 500 mg dose. Ciprofloxacin has a relatively short elimination half life (t1/2=4 h), therefore, a slow-release formulation could reduce variations in the therapeutic effect and so improve its clinical efficacy [6]. The sustained release dosage form has a disadvantage of reduction in absorption as the tablet passes down the GIT [7,8] but this is overcome using the floating tablet.

Previous researchers have shown that in the formulation of Floating tablets that formulation variables like polymer type, polymer ratio, polymer concentration, and sodium bicarbonate concentration have significant effect on release rate, cumulative release and floating lag time, but not on floating duration [7,8].

*Sida acuta* gum is derived from the powdered dried leaves of *Sida acuta* by isopropyl alcohol precipitation of the filtrate from its maceration in distilled water [9]. *Sida acuta* gum was used in tablet formulations as binder, [10] as hydrophilic polymer matrix, [11] and as suspending agent in formulation of paracetamol suspensions [12].

This study was carried out to formulate and evaluate floating matrix tablets of ciprofloxacin in using *Sida acuta* gum as the hydrophilic polymer.

**Materials and Methods**

**Materials**

Chemicals used were of analytical grade, they include; ciprofloxacin,
Sida acuta gum was isolated from the leaves of Sida acuta collected from the botanical garden of Faculty of Pharmacy, Delta State University, Abraka.

**Isolation and purification of Sida acuta gum**

Fresh Sida acuta leaves were sun dried and milled. The method of Okafo and Chukwu [8] was used in the isolation of the gum. The purified gum was dried in an oven (Vego instruments, Mumbai India) at 40°C for 8 h. The dried gum was pulverized and screened using a 300 μm stainless steel sieve. The gum was stored in a dry, air-tight container.

**Pre-compression evaluation**

Ciprofloxacin powder and the excipients were mixed properly and evaluated for their flow properties using their bulk and tapped densities as parameters.

- **Bulk and tapped densities:** A 10 g quantity of the powder blend from each of the formulations was weighed and transferred into a measuring cylinder. The volume occupied was recorded as the bulk volume. Thereafter, the measuring cylinder was tapped 100 times on a padded surface and the new volume occupied was recorded as the tapped volume. This process was repeated twice for all the formulations. The tapped and bulk densities were calculated using equations 1 and 2 respectively.

\[
\text{Bulk density} = \frac{\text{Weight of powder blend (g)}}{\text{Bulk volume (ml)}}
\]

\[
\text{Tapped density} = \frac{\text{weight of powder blend (g)}}{\text{Tapped volume (ml)}}
\]

- **Carr’s compressibility index:**

\[
\text{Carr’s index} = \frac{\text{tapped density} - \text{bulk density}}{\text{tapped density}} \times 100
\]

- **Hausner’s ratio:**

\[
\text{Hausner’s ratio} = \frac{\text{tapped density}}{\text{bulk density}}
\]

## Preparation of ciprofloxacin floating matrix tablets

Direct compression method was used in the preparation of the ciprofloxacin floating matrix tablets using the formula (Table 1). Ciprofloxacin powder was mixed with different concentrations of polymer (Sida acuta gum, HPMC, or NaCMC), MCC, sodium bicarbonate and citric acid. The powder mix was properly blended, thereafter magnesium stearate and talc were added with slight blending. The powder blend was compressed into tablets using a single punch thereafter magnesium stearate and talc were added with slight blending.

## Post-compression evaluation

- **Uniformity of weight:** Twenty tablets were randomly selected and weighed individually. The mean weight of the tablets and the deviation from the mean for each tablet were calculated and recorded.

- **Thickness, diameter and hardness tests:** Six tablets from each formulation were selected at random and inserted individually into the tablet chamber of a digital tablet hardness test apparatus (DIGITAB model, Vego instruments, Mumbai, India). The hardness, thickness and diameter values displayed were recorded.
Zero order model

\[ C = K_0 t \]  \hspace{1cm} (7)

where \( C = \% \) Release, \( K_0 = \) Zero Order rate constant expressed in units of concentration/time (t).

First order model

\[ \log C_r = \log C_0 - \frac{K_r t}{2.303} \]  \hspace{1cm} (8)

where \( C_r = \% \) Remaining, \( C_0 = \) Initial concentration of drug, \( K_1 = \) First Order constant, \( t = \) Time.

Higuchi’s square root law model

\[ Q = K H \sqrt{t} \]  \hspace{1cm} (9)

where \( Q = \% \) Released, \( K_H = \) Constant reflecting design variables of the system, \( t = \) Time.

Hixson–Crowell’s cuberoot law model

\[ \left( \frac{100 - f/100} {n} \right) \sqrt[3] {t} = 1 - K_{HC} t \]  \hspace{1cm} (10)

where \( f = \% \) Released, \( K_{HC} = \) Rate constant, \( t = \) Time.

Korsmeyer–Peppas model

\[ M_t / M_\infty = K t^n \]  \hspace{1cm} (11)

\[ \log M_t / M_\infty = \log K + n \log t \]  \hspace{1cm} (12)

Where, \( M_t / M_\infty \) is the fraction of drug released at time \( t \), \( k \) is the rate constant and \( n \) is the release exponent. The \( n \) value is used to characterize different release mechanisms for cylindrical shaped matrices [17-19].

Results and Discussion

Bulk and tapped densities of ciprofloxacin–excipients blend

The results in Table 2 showed that Carr’s index values of the formulations ranged from 29.00 ± 0.46 to 43.00 ± 0.78, while their Hausner’s ratio was from 1.40 ± 0.02 to 1.74 ± 0.01. According to the specifications in British Pharmacopoeia (2012), the values for formulations CF1 and CF5 indicated poor flow, while CF2 and CF4 had very poor flow. However, their flow could be improved upon by the addition of glidants such as aerosil or talc, or augmentation of their feeding through the hopper. The values for formulation CF3 showed a very, very poor flow. However, their flow could be improved upon by the specifications in British Pharmacopoeia (2012), the values for formulations ranged from 29.00 ± 0.46 to 43.00 ± 0.78, while their Hausner’s ratio was from 1.40 ± 0.02 to 1.74 ± 0.01. According to

Table 1: Composition of floating matrix tablets of ciprofloxacin.

| Ingredients          | CF1     | CF2     | CF3     | CF4     | CF5     |
|----------------------|---------|---------|---------|---------|---------|
| Ciprofloxacin (mg)   | 250     | 250     | 250     | 250     | 250     |
| Sida acuta gum (mg)  | 120     | 180     | 90      | -       | -       |
| HPMC (mg)            | -       | -       | 90      | 120     | 120     |
| Sodium bicarbonate (mg) | 100    | 100     | 100     | 100     | 100     |
| Citric acid (mg)     | 30      | 30      | 30      | 30      | 30      |
| Magnesium stearate (mg) | 6     | 6       | 6       | 6       | 6       |
| Talc (mg)            | 12      | 12      | 12      | 12      | 12      |
| Total (mg)           | 600     | 600     | 600     | 600     | 600     |

USP limit of (90-110%). Proper mixing of powders for granulation or compression leads to less variation in tablet weights and also in drug content.

Buoyancy test: The floating lag time for CF1, CF3 and CF4 as shown in Table 4 was between 1 and 3 min. This indicated excellent floating lag time. CF5 had a floating lag time of 14 min while it took CF2, 1.5 h to float. This shows that formulation CF2 may be expelled from the stomach before it starts floating and this may lead to failure of the dosage form. The buoyancy time for all the formulations was above 12 h.

Swelling study: Figure 1 showed that ciprofloxacin formulation that contained HPMC as the hydrophilic matrix (CF4) swells very fast, almost 5000% of its initial weight within 1 h. Ciprofloxacin tablets from the other formulations swell just above 2000% of their initial weight. After 4 h, the formulation that contained NaCMC (CF5) swells up to 4000% of its initial weight. Formulation CF3 that contains SAG/NaCMC (15%/15%) had a higher swelling capacity than the formulations that contained only SAG (CF1 and CF2).

The tablet formulations were also evaluated based on their swelling abilities. Swelling is a phenomenon that shows a hydrated polymer’s hydrophilicity and ionization of its functional group; this therefore, controls the characteristics of the formed network structure. The swelling index describes the extent of the absorption of water within the hydrated polymer at equilibrium [20].

In vitro drug release: The results in Figure 2 showed that formulation CF1 would not be good as a sustained release formulation as it released more than 70% of its drug content within one hour. CF2 and CF5 released about 70% of their drug content in 6 h which showed moderate sustained release property. CF3 and CF4 released less than 70% of their drug content in 6 h though unlike CF4, CF3 released about 100% of its drug content in 7 h. This showed that SAG at a concentration of 30% or in combination with HPMC (15%/15%) could be used to formulate sustained release ciprofloxacin floating matrix tablets that are comparable to those formed using standard hydrophilic polymers, HPMC and NaCMC.
**In vitro mechanism and kinetics of release:** Formulation CF1 was not able to sustain the release of the ciprofloxacin content; therefore it could not fit well into any of the kinetic release models. The zero order model was the predominant kinetics of release for formulations CF2 and CF5, though first order and Hixson – Crowell model still contributed to the release of formulation CF2. Hixson - Crowell model was the prevalent kinetics of release for formulation CF3. Higuchi model was the predominant release model for formulation CF4 (Table 5).

The mechanism of release using the n – value from Korsmeyer – Peppas model was by super case II transport for formulations CF1 and
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