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# Formulation and *In Vitro* Evaluation of Ofloxacin Tablets using Natural Gum as a binders

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## ABSTRACT

Natural gums are economic, easily available and found useful as tablet binder. In the present investigation, an attempt was made to formulate ofloxacin tablets using three natural binders namely Acacia Arabica; Hibiscus esculentus and Xanthan gum. Such six batches of ofloxacin tablets were prepared using different type and amount of natural binders by wet granulation method. The tablets were analyzed for their hardness, friability, weight variation, and an *in-vitro* release was performed in phosphate buffer at pH 6.8. The prepared tablets were also evaluated for various release kinetic and similarity factor $f_2$. The physical properties of tablets containing natural binders showed sufficient hardness, desirable disintegration time and low friability. The better percentage of drug released was observed as compared to marketed formulation showing more than 85% drug release within 45 minutes. The *in vitro* release data was well fit in to zero order and the values of release exponent 'n' are between 0.303 and 0.514. The high similarity factor $f_2$ of 64.50 was achieved with the best batch in comparison to the marketed tablets. Results obtained indicated that gum Acacia Arabica performed as good as gelatin and to other binders for ofloxacin tablets formulation.

**Key words:** Tablets . Natural binders . Physico-chemical parameters . Release kinetics . Similarity factor

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## Introduction

Tablets, due to their portability and convenience are the most widely prescribed dosage forms in the world. One major class of excipients that is used to improve tablet formulations is the pharmaceutical binders or some time referred as adhesive [1]. Binders are pharmaceutical excipient that are commonly employed in tablet formulation to impart cohesion on the powder mixture and hence improves on the flow properties on the granules. Binders act by causing aggregation of powders thereby forming granules through the process of granulation [2]. Natural polysaccharides are widely used in the pharmaceutical and food industry as excipients and additives due to their low toxicity, biodegradable, bio competitive, availability and low cost. Natural binders like different starches, gums, mucilages, dried fruits possess binding capacity as well as some other properties like disintegrant, filler, sustain release, and these natural polymers are much safer and economical than polymers like polyvinylpyrrolidone (PVP) [3, 4]. *Acacia arabica* (Lam.) Willd (Family : Mimosaceae), commonly known as babul, kikar or Indian gum. Arabic tree has been recognized worldwide as a multipurpose tree and it is widely distributed throughout arid and semi-arid zones of the world [5]. *Hibiscus esculentus L*. (Family: Malvaceae), commonly known as bhindi in India, krajiab kheaw in Thailand, okra plant, kopi arab, kacang bendi and bhindi in South East Asia, a tropical to subtropical plant that is widely distributed from Africa to Asia, Southern European and America. Okra plays an important role in the human diet by supplying fats, proteins, carbohydrates, minerals and vitamins. Moreover, its mucilage is suitable for certain medical and industrial applications [6]. Xanthan gum is another natural, biosynthetic, edible gum and an extracellular polysaccharide produced by the bacterium Xanthomonas campestris. Zanthan gum consists of glucose, mannose, and glucuronic acid and is used in different foods as thickener and stabilizer [7].

Ofloxacin is a synthetic chemotherapeutic antibiotic of the fluoroquinolone class considered to be a second-generation fluoroquinolone. It is used to treat mild to moderate urinary tract infections, prostatitis, lower respiratory tract infections, and skin infections [8]. The aim of the present work is to prepare tablets using three different types of natural polymers namely Acacia Arabica, Hibiscus esculentus and xanthan gum and to evaluate these formulations for different physical parameters. The influence of different types and amounts of binders both on the tablet quality (i.e. crushing strength, friability, disintegration time and dissolution time) were investigated.

## Experimental

### *Materials*

Ofloxacin was obtained as gift sample from, Loba, Pharmaceuticals and Chemicals Ltd, Mumbai. Carboxy methyl cellulose, Di-calcium phosphate, Magnesium stearate, Talc and other chemicals were procured form Loba, Pharmaceuticals and Chemicals Ltd, Mumbai. Acacia Arabica; Hibiscus esculentus; Xanthan gum were procured from local market. OF® (Marketed formulation) was purchased from local market.

### *Methods*

### *Preparation of Tablets*

Ofloxacin tablets were prepared by wet granulation technique [9]. All the ingredients were grinded properly using a mortar pestle. The composition of different batches for preparation of tablets using different binder with fixed amount of drug is shown in Table 1. Required quantity of drug, binder, disintegrate and diluents were passes through 40# sieve separately and then mixed uniformly by methanol as granulating agent to get a coherent wet granulate which was screened through 16 # sieve to obtain coarse granules followed by drying of granules at $45^0$C for 1 hour. The dried granules were then passed through the 20 # sieve and were lubricated with magnesium stearate and talc. Finally, the dried granules were compressed as tablets using Mini-Press compression machine.

**Tab. 1.** Composition of Ofloxacin tablets containing different gum as binder.

| **Ingredients** | **Formulations (mg)** | | | | | |
|---|---|---|---|---|---|---|
| | **F1** | **F2** | **F3** | **F4** | **F5** | **F6** |
| Ofloxacin | 200 | 200 | 200 | 200 | 200 | 200 |
| Acacia Arabica | 7.5 | 15 | ---- | | ---- | |
| Hibiscus esculentus | ---- | | 7.5 | 15 | ---- | |
| Xanthan gum | ---- | | ---- | | 7.5 | 15 |
| Corboxymethyl cellulose | 15 | 15 | 15 | 15 | 15 | 15 |
| Di calcium phosphate | 74 | 66.5 | 74 | 66.5 | 74 | 66.5 |
| Magnesium streate | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 |
| Talc | 2.5 | 2.5 | 2.5 | 2.5 | 2.5 | 2.5 |

Total weight of each tablet = 300 mg

***Characterization of the Tablet***

The prepared tablets were evaluated for various parameters like physical appearance, hardness, friability and disintegration time according to the USP 29 requirements [10, 11] and is shown in Table 2. The tablets were evaluated for hardness using Monsanto hardness tester. The hardness reported is an average of three measurements. Twenty tablets were weighed and placed in a friabilator. After rotating for 4 min that is 100 revolutions, the percentage loss of weight was determined as an indicator of friability. The disintegration test was performed in water at $37^0$C. The disintegration time reported is an average of three determinations.

**Tab. 2.** Evaluation of Various Parameters of Ofloxacin Tablets

| Batch | Thickness (mm) | Diameter (cm) | Weight variation (mg) | Hardness (N) | Friability (%) | Disintegration time (min) |
|---|---|---|---|---|---|---|
| F1 | 4.054 ± 0.04 | 0.89 ±0.09 | 0.3015 ± 0.01 | 29.421 ± 3.4 | 0.3330 ± 0.02 | 21 ± 2.2 |
| F2 | 4.051 ± 0.02 | 0.89 ± 0.09 | 0.2987 ± 0.02 | 39.23 ± 2.1 | 0.2212 ± 0.01 | 16 ± 1.3 |
| F3 | 4.052 ± 0.07 | 0.89 ± 0.08 | 0.3017± 0.01 | 22.77 ± 2.7 | 0.3333 ± 0.02 | 13 ± 2.2 |
| F4 | 4.055 ± 0.03 | 0.89 ± 0.07 | 0.3008 ± 0.01 | 34.16 ± 3.1 | 0.3101 ± 0.02 | 21 ± 1.7 |
| F5 | 4.055 ± 0.04 | 0.89 ± 0.10 | 0.2995 ± 0.01 | 41.12 ± 3.3 | 0.3332 ± 0.02 | 25 ± 1.6 |
| F6 | 4.053 ± 0.02 | 0.89 ± 0.07 | 0.3017 ± 0.02 | 45.23 ± 3.5 | 0.2315 ± 0.01 | 32 ± 2.4 |

All values are expressed as mean ± SD, n = 3.

***In vitro dissolution study***

Dissolution rate of Ofloxacin from various tablets was studied using USP XXIII six-station dissolution test apparatus (Electrolab, INDIA) with paddle stirrer. The dissolution rate was

studied by placing one tablet containing 300 mg Ofloxacin in 900 ml of phosphate buffer of pH 6.8 maintained at 37±0.5$^0$C with a speed of 50 rpm. Samples of 5 ml were withdrawn at different time intervals, filtered (though 0.45 µ) and replaced with 5 ml of fresh dissolution medium. The samples were properly diluted and estimated spectrophotometrically at 207 nm by using ELICO double beam UV spectrophotometer [12]. *In vitro* release profile of Ofloxacin tablets containing different natural binders is shown in Figure 1.

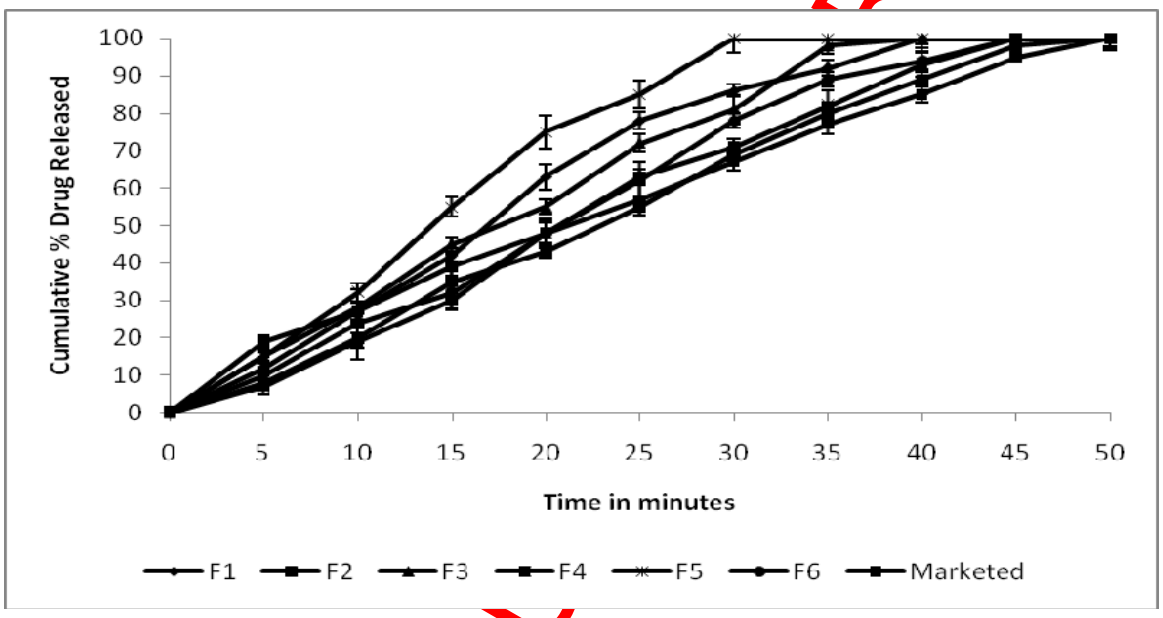


**Fig. 1.** *In vitro* release profile of Ofloxacin from tablets containing different natural binders. Values are mean ± SD ($n$ = 3).

***Data Analysis***

The results of the *in vitro* drug release study were fitted with various kinetic equation like zero order (% release vs time), first order (log % unreleased vs time), Higuchi matrix (% release vs square root of time). In order to define a model which will represent a better fit for the formulation, drug release data further analyzed by Peppas equation, $M_t/M_\infty = k\ t^n$, where $M_t$ is the amount of drug released at time 't' and $M_\infty$ is the amount released at time '∞', the $M_t/M_\infty$ is the fraction of drug released at time 't', 'k' is the kinetic constant and 'n' is the diffusional exponent, a measure of the primary mechanism of drug release. $R^2$ values were calculated for the linear curves obtained by regression analysis of the above plots [13]. The similarities between two dissolution profiles were assessed by a pair-wise model independent procedure such as similarity factor ($f_2$) [14]:

$$f_2 = 50 \times \log\left\{\left[\left(1+\frac{1}{n}\right)\sum_{t=1}^{n}(R_t - T_t)^2\right]^{-0.5} \times 100\right\}$$

Where, 'n' is the number of pull points, $w_t$ is an optional weight factor, $R_t$ is the reference profile at time point 't', and $T_t$ is the test profile at the same time point; the value of $f_2$ should be between 50 and 100. An $f_2$ value of 100 suggests that the test and reference profiles are identical and, as the value becomes smaller, the dissimilarity between release profiles increases [15]. The above values are summarized in Table 3.

**Tab. 3.** Various parameters of the model equations and similarity factor on the *in vitro* release kinetics.

| Kinetic Model | F1 | F2 | F3 | F4 | F5 | F6 | Marketed Tablet |
|---|---|---|---|---|---|---|---|
| Zero Order | 0.92 | 0.99 | 0.941 | 0.979 | 0.851 | 0.97 | 0.991 |
| Higuchi | 0.83255 | 0.972 | 0.9531 | 0.987 | 0.9012 | 0.8742 | 0.9621 |
| First order | 0.973 | 0.822 | 0.7661 | 0.913 | 0.976 | 0.9242 | 0.87 |
| Peppas | 0.807 | 0.877 | 0.861 | 0.849 | 0.74 | 0.875 | 0.946 |
| 'n' value | 0.303 | 0.434 | 0.596 | 0.428 | 0.49 | 0.514 | 0.47 |
| $f_2$ Value | 43.21 | 64.50 | 46.10 | 57.31 | 33.72 | 55.62 | -- |

## Results and Discussion

A large number of natural polymers have been used in pharmaceutical preparations. Natural substances like starches, mucilages, gums and dried fruits have been used as binding agent. In the present study, three natural binders namely Acacia Arabica; Hibiscus esculentus and Xanthan gum were used to prepare Ofloxacin tablets. Tablets were prepared with two different amounts of binders and evaluated for different physicochemical parameters as shown in Table 2. It can be seen from the results that as the amount of binder increases the hardness and disintegration time increased and decreased in friability values of the tablets. This finding may be attributed to gel forming property of gum present in the tablet matrix in line with the similar results reported earlier [1, 16]. The hardness of the tablet varies between 22 and 45 N clearly indicating that they are strong tablets and they can withstand the mechanical shocks. This is combined with the friability (less than 1%) of all the formulations demonstrated the effectiveness of the gum for use as binder. In general, the tablet hardness between 40-50 Newton, friability less than 1% and the disintegration time less than 30 minute

lied in pharmacopoeial limits [17]. It was observed from Table 2, that all formulations are in an acceptable levels [10].

The dissolution profile of the prepared tablets is shown in Figure 1. The drug release profiles were found to be similar despite of the varying type of binder and physicochemical characteristics of the excipients. It was found that the drug release was decreased with increase in concentration of gum. All the batches indicated better drug release profile and showed more than 85% within 45 min from the tablets prepared using different type and amount of binder.

The release exponent '*n*' and $R^2$ values for the formulations are given in the Table 3. It can be seen from the data analysis of release profiles according to different kinetic models highest correlation was observed with zero order as compared to other models. The tabulated data showed that values of 'n' are between 0.303 and 0.514. This implies that the release mechanism is Fickian and not much variation was observed in the 'n' value.

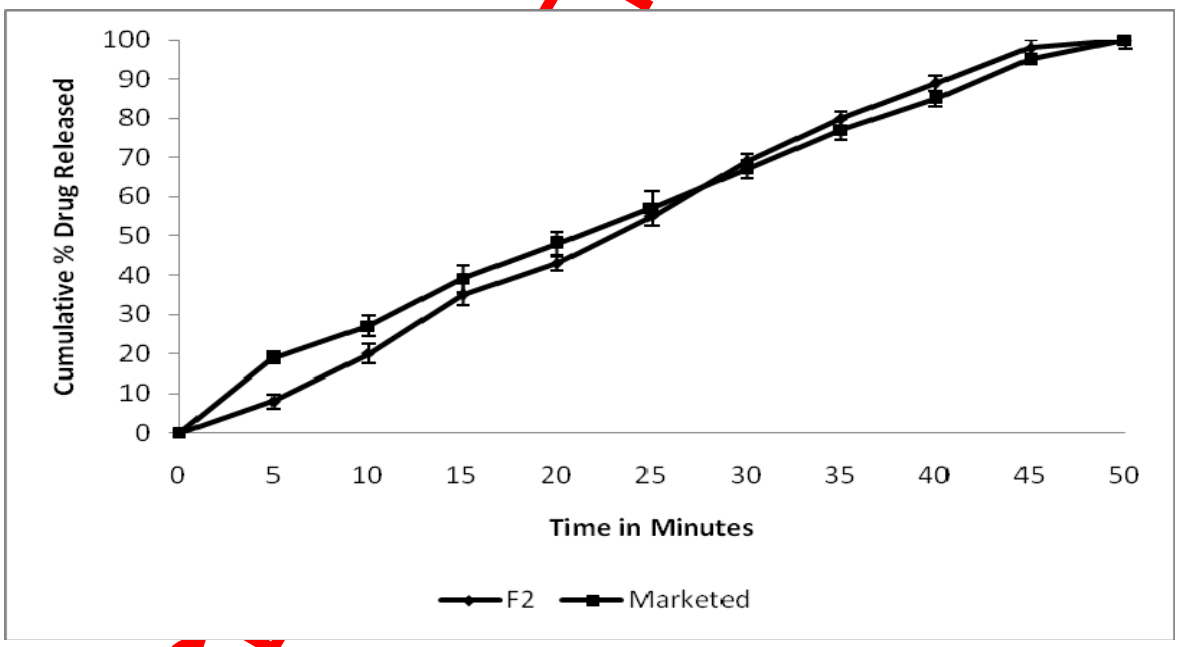


**Fig. 2.** Comparison of *In vitro* release profile of selected batch (F2) with marketed tablet. Values are mean ± SD ($n = 3$).

Among all the formulations F2 showed the best physicochemical parameters and release profile as compared to other formulations. The release profile of selected batch was compared

with the marketed preparation (OF®) of as shown in Figure 2. It can be observed that the release profile of tablet prepared using Acacia Arabica as natural binders have similar release characteristics to that of the commercially available formulation. The similarity factor $f_2$ was a logarithmic transformation of the sum-squared error of differences between the experimental drug release $T_t$ and the ideal release $R_t$ for over all time points 'n'. The similarity factor fit the result between 50 and 100. It approached '0' as the dissimilarity of the test and the reference profile increased, whereas, it attained 100 when the test and the reference profile were identical [18]. In the present study, the value for the similarity factor ($f_2$) for all the prepared batches was observed in the range of 33 to 64. It is evident from the results that batches F1, F3 and F5 did not fulfill the above criteria. The highest value was observed with batch F2 (64.50) which was more comparable to that with the marketed formulation suggesting that the dissolution profile of the selected formulation (F2) and marketed formulation are similar.

## Conclusions

Ofloxacin tablets were successfully prepared using three different natural binders (Acacia Arabica; Hibiscus esculentus and Xanthan gum) which were evaluated for their physicochemical parameters and drug release studies. Among the studied natural binders *Acacia Arabica* was more comparable to Hibiscus esculentus and Xanthan gum in terms of drug release and similarity factor in relation to the marketed formulation. Hence, it is concluded that *Acacia Arabica* could be used as a binding agent for the formulation of Ofloxacin tablet. Further, Acacia Arabica can substitute more expensive binders. Therefore, *Acacia Arabica* as natural material can be widely used in the field of drug delivery because, they are readily available, cost effective, eco-friendly, capable of multitude of modifications, potentially degradable and compatible due to their natural origin.

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## References

[1] Tavakoli N, Ghassemi DN, Teimouri R, Hamishehkar H. Characterization and evaluation of *okra gum* as a tablet binder. Jun J Natural Pharm Prod. 2008; 3(1): 33-38.

[2] Singh AK, Shingala VK, Panner SR, Sivakumar T. Evaluation of *mangifera indica gum* as tablet binder. Inter J Pharm Tech Res. 2010; 2(3): 2098-2100.

[3] Patel S, Agrawal S, Singh LB. Natural binding agents in tablet formulation. Inter J Pharm & Bio Arch. 2012; 3(3): 466-473.

[4] Kulkarni U, Patil BS, Korwar PG. Evaluation of *tapioca sago starch* as a binder in tablet formulation. J Pharm and Herbal Form. 2010; 1(1): 1-8.

[5] Rajvaidhya S, Nagori BP, Singh GK, Dubey BK, Desai P, Jain S. A review on *Acacia arabica* - An indian medicinal plant. Inter J Pharm Sci and Res. 2012; 3(7): 1995-2000.

[6] Ali EM, Fazel NS, Nabavi SM, Eslami B. Antihypoxic and antioxidant activity of *Hibiscus esculentus* seeds. Grasas Y Ceites. 2010; 61 (1): 30-36.

[7] Talukdar MD, Mahiuddin, Jacqueline PV. Evaluation of *xanthan gum* as a hydrophilic matrix for controlled-release dosage form preparations. Drug Devel and Ind Pharm. 1993; 19(9): 1037-1046.

[8] Monk JP, Deborah MCR : A review of its antibacterial activity, pharmacokinetic properties and therapeutic use. Drugs. 1987; 33(4): 346-391.

[9] Prasanthi NL, Manikiran SS, Rama RN. *Invitro* drug release studies of *ziprasidone* from tablets using natural gums from biosphere. Arch Appl Scie Res. 2011; 3 (2): 513-519.

[10] Brater C. The United States Pharmacopoeia (USP 29)/National Formulary (NF 24). The United States Pharmacopeial Convention, Rockville, USA, 2006: 2503-2508, 2597, 3046.

[11] Lachman L, Lieberman HA, Kanig JL. The Theory and practice of Industrial pharmacy. Varghese publishing House, Mumbai; 2009, p. 317.

[12] Chavanpatil M, Jain P, Chaudhari S, Shear R, Vavia P. Development of sustained release *gastroretentive* drug delivery system for : *In vitro* and *in vivo* evaluation. Inter J Pharm. 2005; 304(1–2): 178-184.

[13] Nagda CD, Chotai NP, Nagda DC, Patel SB, Patel UL. Preparation and characterization of spray-dried mucoadhesive microspheres of *ketorolac* for nasal administration. Cur Drug Delivery. 2012; 9(2): 205-218.

[14] Gowda DV, Manjunatha M, Balmurlidhara V, Khan MS. Study on encapsulation of *Ranolazine* in bees wax microspheres: Preparation, characterization and release kinetics

of microspheres. Der Pharmacia Lettre. 2010; 2(6): 232-243.

[15] Varshosaz J, Tavakoli N, Kheirolahi F. Use of hydrophilic natural gums in formulation of sustained-release matrix tablets of *tramadol hydrochloride*. AAPS Pharm Sci Tech. 2006; 7(1): E1-E7.

[16] Panda DS, Choudhury NSK, Yedukondalu M, Gupta R. Evaluation of gum of *Moringa oleifera* as a binder and release retardant in tablet formulation. Ind J Pharm Sci. 2008; 70(5): 614-618.

[17] The Indian Pharmacopoeia, Vol. II, Govt. of India, Ministry of Health and Family Welfare. The Controller of Publication, New Delhi, 1996.

[18] Sahoo NG, Kakran M, Lin L, Judeh Z. Fabrication of composite microparticles of *artemisinin* for dissolution enhancement. Powder Technology. 2010; 203: 277-287.