
Application of *Abelmoschus esculentus* Gum as a Mini-Matrix for Furosemide and Diclofenac Sodium Tablets

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A gel forming polysaccharide gum obtained from the pods of *Abelmoschus esculentus* was employed as a mini matrix in a new sustained release tablet formulations of furosemide (a diuretic) and diclofenac sodium (a non steroidal anti inflammatory agent). Sustained release performance of the formulations was compared with formulations containing sodium carboxymethylcellulose (NaCMC, 500 mPa) in similar experimental conditions. *Abelmoschus esculentus* gum was as good as NaCMC in prolonging the release of furosemide and diclofenac sodium from the compressed tablets. Times for 50% ($t_{50\%}$) and 75% ($t_{75\%}$) indicated relatively faster release of furosemide in simulated intestinal fluid (SIF). Similar trends are observed in the case of diclofenac sodium. A reduction in the solubility of diclofenac sodium was observed and this was caused by the presence of sodium and potassium in SIF. These new formulations which utilize a plant hydrogel as mini matrix offer the advantage of simplicity and economy.

Plant hydrocolloids have been evaluated extensively as hydrophilic matrices for sustained release drug delivery systems¹⁻⁴. Gum extract from the pods of *Abelmoschus esculentus* was evaluated for its binding potential in sulphaguanidine tablets⁵. In the present study the gum was employed as mini-matrix in the formulations of furosemide and diclofenac sodium tablets intended for sustained release action. Furosemide and diclofenac sodium were used as test drugs because they possess the desirable properties necessary for sustained release formulation and their sustained release formulations were reported earlier^{6,7}.

The following materials were used as procured from their manufactures: diclofenac sodium (Ciber Geigy, Switzerland), furosemide (Hoechst, Germany), lactose (May and Baker, England), magnesium stearate (Merck, Germany), sodium carboxymethylcellulose 500 mPa (Fluka, Germany). All other chemicals were of Analar grade. *Abelmoschus esculentus* gum was extracted from fresh pods of *A. esculentus* by the method reported previously⁵.

Each tablet of furosemide contained 80 mg of furosemide, 10% w/w. *A. esculentus* gum, 1% w/w magnesium stearate and enough quantity of lactose to obtain a 300 mg tablet, while each tablet of diclofenac sodium contained 50 mg of diclofenac sodium 10% w/w of *A. esculentus* gum, 1% magnesium stearate and enough quantity of lactose to obtain a 300 mg tablet. The tablets were prepared using a slight modification of the wet granulation method previously reported⁸. In each case, the drug was mixed with the lactose in a mortar. *A. esculentus* gum was dissolved in predetermined volume of distilled water heated to 60°. The gum dispersion was incorporated into the drug-lactose mixture by trituration using a pestle after cooling the mucilage to room temperature of 30 ± 1°. Trituration of the mixture was continued until a damp mass suitable for screening through a 1.70 mm stainless steel sieve was achieved. Screened wet granules were dried for 6 h in a hot air oven set at 50°. Dried granules were screened through a 1.0 mm stainless steel sieve and stored in amber coloured specimen bottles. Furosemide and diclofenac sodium granules containing 10% sodium carboxymethylcellulose and that containing 0% polymer were similarly prepared.

The granules were compressed in a F-3 Manesty Single Punch electric tableting machine (Manesty, Eng-

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land) fitted with 0.95 cm flat faced punches. Tablet target weight was 300 ± 5 mg and the compression load was set at 490 kg. Granules were lubricated with 1% magnesium stearate previously screened through a 0.20 mm stainless steel sieve prior to compression. A total of 250 tablets were compressed per batch. Tablets were stored in amber coloured bottles tightly closed to exclude moisture.

The tablet batches were evaluated for hardness and friability after 72 h post compression, disintegration time after 96 h and dissolution profile studies after one week post compression. For each tablet batch, hardness of ten tablets were individually measured using the Monsanto hardness tester, while ten tablets from each batch were dedusted and subjected to abrasive shock in an Erweka friabilator (TAR Model) to assess their friability. Percent loss in weight represents the friability for each batch of tablet. Tablet disintegration was assessed in simulated intestinal fluid (SIF) without pancreatin with the Manesty single unit disintegration assembly (TD88 T175 model). The dissolution properties of the tablets were assessed using the Erweka dissolution apparatus (DT-D model) fitted with a paddle that was operated at a revolution of 50 ± 1 rpm. The dissolution medium in each case was a 1000 ml SIF maintained at $37 \pm 1^\circ$. The choice of SIF was based on the solubilities of the two drugs. A 10 ml volume was withdrawn with a 10 ml pipette fitted with a non-absorbent cotton wool at predetermined time intervals. A 10 ml volume of SIF maintained at the same temperature was added to the dissolution medium immediately after each withdrawal. Withdrawn samples were diluted appropriately with SIF and their absorbance values were read at 273 nm and 266 nm for furosemide and diclofenac sodium respectively in a spectronic 120 (Milton Roy, Germany) spectrophotometer. Absorbance values were converted to concentration using the Beer's calibration curves previously constructed for the two drugs. Points plotted are average of two replicate determinations.

Values obtained were very close and standard deviations were omitted from the plotted points for the purpose of clarity.

Abelmoschus esculentus gum conferred good mechanical properties to both furosemide and diclofenac sodium tablets as evidenced by zero friability obtained with tablets of both drugs. Relatively higher hardness values were obtained for furosemide tablets containing *A. esculentus* gum the diclofenac sodium tablets containing the same concentration of *A. esculentus* (Table 1). As could be seen in Table 1, tablets with relatively higher hardness values were obtained with NaCMC in the two dosage forms under consideration. The differences observed in the hardness of tablets of the two drugs may be related to the inherent compressibility of the two drugs. The two batches of tablets containing no polymer produced weak and highly friable compacts, their properties were therefore omitted. The tablets were non disintegrating after 1 h but did swell appreciably in SIF.

The dissolution profiles of furosemide and diclofenac sodium are shown in figs. 1 and 2. The releases of furosemide and diclofenac sodium were almost complete within 6 h. There were, however, slight difference in the dissolution profiles of the two drugs in SIF in presence of *A. esculentus* or sodium carboxymethylcellulose.

The time for 50% release ($t_{50\%}$ value) of furosemide and diclofenac sodium from tablets containing *A. esculentus* are not significantly different (Table 1). There were, however, a significant difference in the time for 75% of drug release ($t_{75\%}$ value) of furosemide and diclofenac sodium. The initial fractional releases (based on fractional releases versus time plots) were 0.15 for furosemide and 0.10 for diclofenac sodium. This fractional release, f_1 , represents the fraction of each drug that was released immediately and which was expected to provide initial activity of the drug *in vivo*. After the initial fraction release, f_1 , other fraction, f_2 , released

TABLE 1: SOME *IN VITRO* PROPERTIES OF FUROSEMIDE AND DICLOFENAC SODIUM TABLETS

Parameter	Furosemide		Diclofenac sodium	
	Ae	NaCMC	Ae	NaCMC
Hardness (kgf)	7.61±0.62	9.10±1.45	6.78±1.11	7.70±1.57
t_{50} (h)	1.20	1.65	1.25	1.40
t_{70} (h)	1.70	2.65	2.30	2.30

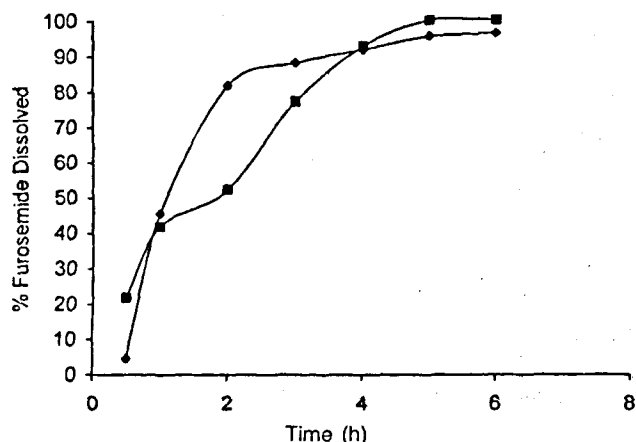


Fig. 1: Release profile of furosemide from tablets.

Release of furosemide from tablets containing 10% w/w *A. esculenta* (-◆-) or with 10 % w/w NaCMC (-□-) into simulated intestinal fluid was determined spectrophotometrically.

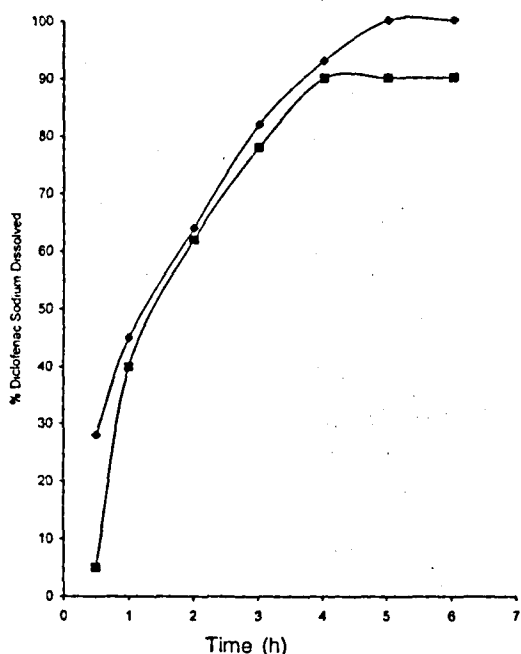


Fig. 2: Release profile of diclofenac sodium from tablets.

Release of diclofenac sodium from tablets containing 10% w/w *A. esculenta* (-◆-) or with 10 % w/w NaCMC (-□-) into simulated intestinal fluid was determined spectrophotometrically.

followed exponential function and the amount of both drugs released (a_t) at any time could be estimated from Equation 1:

$$a_t = a_0 f_1 + a_0 f_2 (1 - e^{-kt}) \dots \dots 1.$$

where a_0 is the amount of drug loaded and k is the release constant. It is evident from the fraction of drug released f_1 , that furosemide was released relatively faster from *A. esculenta* gum mini-matrix than diclofenac sodium. The difference in the $t_{75\%}$ values shown in Table 1 apparently resulted in apart from the differences in the solubility of the two drugs in alkaline solution of SIF and on the rate of fluid penetration into the tablets. Furosemide has poor aqueous solubility but is readily soluble in alkaline solution¹⁰. The aqueous solubility of diclofenac sodium on the other hand is dependent on pH. Its solubility is poor at low pH but when the pH rises above the pK_a , rapid increase in solubility occurs¹¹. Thus in SIF, the release of furosemide or diclofenac sodium involved the sequential processes of SIF infiltration into the matrix, hydration and swelling of the matrix, dissolution of furosemide or diclofenac sodium in the matrix, and then leaching of the solubilized drugs through the interstitial channels. This process can be described by the well known Higuchi's Equation that described diffusional release of drugs from swellable polymeric systems. Even though maximum solubility of diclofenac sodium occurs at pH 7.0 and pH 7.5¹², the presence of the cations (sodium and potassium) present in SIF markedly affected its solubility¹⁷.

The $t_{50\%}$ and $t_{75\%}$ of furosemide and diclofenac sodium in the presence of NaCMC show values of 1.65 h ($t_{50\%}$) and 2.65 h ($t_{75\%}$) for furosemide and 1.40 h ($t_{50\%}$) and 2.30 h ($t_{75\%}$) for diclofenac sodium (Table 1). The slight differences in these values could be related more to the differences in the hardness of the tablets and the rate of fluid penetration into them.

Recently published works on sustained release furosemide formulations were based on wax matrix systems^{6,7}. In one of the works, predictable release of furosemide was only achieved using maize starch as a drug release modulator. On the other hand, formulations of sustained release diclofenac sodium based on wax matrix and hydrogels have been reported¹³. Here the release of diclofenac sodium from wax matrix tablet was attributed to diffusion through the pores in the matrix, whereas release from the hydrogel tablets was dependent on the extent of swelling and erosion of the hydrogel. The present formulations of diclofenac sodium and furosemide tablets utilized a plant polysaccharide gum as mini-matrix. This approach offers the advantage of simplicity and economy.

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Extractive Spectrophotometric Determination of Iron as an Impurity in Pharmaceutical Raw Materials

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The objective of the present study is to develop an instrumental method, which is more accurate than the physical method that is followed in Indian Pharmacopoeia. A simple and sensitive spectrophotometric method has been developed for the estimation of iron as an impurity in pharmaceutical raw materials. In this method wine red color complex formed between iron and 1-3-diphenyl-4-carboethoxy pyrazole-5-one (DPCP) was measured at 525 nm. Beer's law was found to obey in the concentration range 0.5-10 µg/ml. Sandell's sensitivity and standard deviations were found to be 0.0483 µg/cm² and ±0.035 respectively.

Concept about purity has changed with time and is indispensable for development in analytical chemistry. Hence detection and estimation of impurity is one of the most important subjects in a pharmaceutical industry. The pharmacopoeia places the greatest emphasis on the control of physiologically harmful impurities. Contamination by arsenic and lead is widespread, largely as a result of atmospheric pollution. Iron is also one of the associated impurities. Iron in trace amount is one of the important constituents of the body metabolism. The

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excess intake of iron may cause siderosis and other toxicological complications. So need arises to limit the presence of iron in raw materials, which are used in pharmaceutical formulations. The chemical test that detects and measures the impurity is called limit test. The limit test of iron is provided to determine that the content of iron as an impurity does not exceed the limit for iron specified in the individual monograph of the pharmacopoeia.

In the existing method given in Indian Pharmacopoeia, the determination of iron is done by concomitant visual comparison with a control, prepared from a