

## Full Length Research Paper

# Encapsulation of indomethacin in calcium alginate-galactomannan hydrogels

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The swelling behaviour of konkoli seed galactomannan (KGS) hydrogels was studied to find their suitability for use in drug delivery. The study involves encapsulation of indomethacin with an alginate-galactomannan hydrogels. The swelling behaviour of the hydrogels systems was found to increase with increase in concentration of galactomannan. The release measurements of the drug from these systems were performed at room temperature (27°C) by standard acid base titration method. The fractional release obtained was affected by galactomannan concentration in the drug formulated matrix which resulted to fast rate of release behaviour. That is 1.0gKGS > 0.8gKGS > 0.5gKGS > NaAlg.S. The formulated hydrogels have potentials that could suggest their use in pharmaceutical industry for drug release in addition to the existing once.

**Keywords:** Konkoli, hydrogels, swelling, indomethacin, release

## INTRODUCTION

Konkoli seed gum (KGS) is a galactomannan obtained from the seed of konkoli plant scientifically identified as *maesopsis eminii*, commonly called musizi in Tanzania (Hall, 1995; Joker, 2000; Rugalema et al, 1994), but locally it is known as 'konkoli' in North Eastern Nigeria. KSG is widely used as thickeners in soup and traditional baked food products in Nigeria, primarily because of its high viscosity, binding and swelling propensity (Barminas and Eromosele, 2002; Osemeahon et al., 2008). This plant is a large Africa tropical forest tree introduce to various parts of the tropics for timber production or as a shade tree (Barminas, 2004). In Nigeria, this plant grows in the wild in the east, south and middle belt of the country (Aliyu, 2002; Osemeahon, 2003; Osemeahon et al, 2008). It's shoots greenish flowers around April and may and bears fruits which get matured around August and September as they become publish black containing a very hard seed. The seed are normally removed from the dry fruits and ground into fine powder and may be constituted in hot or cold water and used in the preparation of soups and other traditional baked foods (Osemeahon, 2003; Osemeahon et al., 2008)

Hydrogels are hydrophilic, three – dimensional networks that possess the ability to swell in aqueous

media without dissolution (Cauich- Rodriguez *et al*, 2001 and Baljit, 2007a). For drug delivery, among hydrophilic polymers, natural polysaccharides are the choice material due to their nontoxicity and acceptance by regulatory authorities (Sumthi and Ray, 2002). For example, hydrogel from tamarind has been used for drug release due to non-carcinogenicity, mucoadhesivity, biocompatibility, high drug holding capacity and high thermal stability (Sumathi and Ray, 2002). In their ability to retain a significant amount of water; hydrogels are quit similar to living tissue, rendering them useful for a wide variety of biomedical applications. (Sumathi and Ray, 2002; Tommansina *et al.*, 2007).

Hydrogels usually exhibit different degrees of swelling depending on their composition and molecular structure. In addition, there is a growing interest in the group of hydrogels that are responsive to changes in their environment such as pH, temperature, or ionic strength. Hydrogels show significant variation in swelling as a result of external changes such as pH and temperature have been investigated for a wide range of application namely controlled release, pH-specific membrane separation, purification of pharmaceutical products, solution separation and solvent recovery (Cauich-Rodriguez *et al.*, 2001).

Among the numerous polymers that have been proposed for the preparation of hydrogels, polysacchari-

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des have a number of advantages over the synthetic polymers which were initially employed in the field of pharmaceuticals (Wichterle and Lim, 1960; Tommansina *et al.*, 2007). Indeed, polysaccharides are abundant and readily available from renewable sources such as the algal and plant kingdoms, cultures of microbial selected strains, as well as through recombinant DNA techniques. Thus, they have a large variety of composition and properties that cannot be easily mimicked in a chemical laboratory, and the ease of their production makes numerous polysaccharides cheaper than synthetic polymers.

In recent years, a number of studies have greatly contributed to our present understanding of polysaccharidic hydrogel networks, with numerous system of this unique class of material being proposed. Apart from their great versatility in modified drug delivery, more recent progresses have been made in the use of hydrogels as matrices for the encapsulation of living cells, as biologically friendly scaffolds for tissue engineering and for the controlled release of proteins (Tommansina *et al.*, 2007).

The number of polysaccharides that have been investigated for the preparation of hydrogels suitable as delivery system is extremely large. These include alginate, carrageenans, dextran, gellan, guar gum, xanthan etc, but up to now no scientific information are currently available on swelling behaviour of hydrogels obtained from konkoli seeds for use in drug delivery. Therefore, the present study is an attempt, to prepare hydrogels from KGS to find their suitability for use in drug delivery in addition to the existing ones. This property if evaluated could promote value addition, serve as commercial polysaccharide gums and create awareness on their potential applications in industries.

## MATERIALS AND METHODS

### Materials

Konkoli (*Maesopsis eminii*) was obtained from Yola market, Nigeria. Sodium alginate and calcium chloride were obtained from British Drug House (BDH). The entire chemicals were of analytical grade and were used as provided.

### Methods

#### Preparation of Calcium Alginate Hydrogel

This was prepared by a standard method described by David and Cooker (2005). Sodium alginate powder 2.5 g was dispersed into 100ml of distilled water to give a 2.5% w/v solution. This solution was then mixed with a magnetic stirrer until a transparent viscous solution obtained. Also 2.6 g calcium chloride was dissolved in 100ml distilled water to give calcium chloride solution. Calcium alginate hydrogel was prepared by pouring the solution of prepared sodium alginate into a glass syringe and titrate drop wise into a continuously and magnetically stirred calcium chloride solution. This

technique enables the formation of transparent spherical gel droplets designated as NaAlg.S.

#### Preparation of Calcium Alginate Galactomannan Hydrogel Systems

Konkoli seed galactomannan (KSG) powder of different weights (0.5 g, 0.8 g, and 1.0 g) and sodium alginate powder 2.5 g were weighed and dispersed separately into 100ml of distilled water to give 0.5, 0.8, 1.0 and 2.5% w/v of galactomannan and alginate solutions respectively. These solutions were mixed with a stirrer until a uniform viscous solution obtained. The galactomannan and sodium alginate were mixed in the ratio of 3:1 with a magnetic stirrer. This solution was poured into a glass syringe. Calcium chloride solution was prepared as in the preparation of calcium alginate above. The calcium galactomannan hydrogels was obtained by titrating drop wise the content of the glass syringe into a continuously and magnetically stirred calcium chloride solution. The gel hydrogels obtained was then designated as 0.5, 0.8, and 1.0kgs according to the weight of the galactomannan used in the hydrogel preparation (Zinge *et al.*, 2001).

#### Encapsulation of Drug (Polysaccharide Matrix Tablet)

A granulation method by Zinge *et al.*, 2001 was adopted. Indomethacin was interacted with the hydrogels obtained from Preparation of Calcium Alginate Galactomannan Hydrogel Systems and Preparation of Calcium Alginate hydrogels above. Dried and finely powder hydrogels weighing 225mg were interacted with a portion of 90mg of indomethacin powder. This was thoroughly mixed and allowed to pass through 60 size mesh sieve three times. The mixture was then hydrated with 3 drops of distilled water. The thick gel obtained after homogenization with a spatula, was air dried on a glass plate and heated to 40°C for 2h in a Shermond Oven (Model 2200). The hydrogels obtained were designated as NaAlg.S, 0.5gKGS, 0.8gKGS and 1.0gKGS.

#### Swelling Measurement

The modified "Tea bag" method by Osemeahon *et al.*, (2003) was employed. A transparent polyethylene bag was employed here and instead of hanging the bag to drain off, a micro-syringe was used to suck away excess solution. The method entailed weighing 0.1 g of each of the samples into a weighed polyethylene bag and reweighed again. 10ml of distilled water was added to the polyethylene bag with the sample inside and hermetically sealed. The bag with its content was then left undisturbed at room temperature (27°C) and at different time intervals ranging from 2min-10hrs. Excess solution was carefully sucked out after a specified time reached. The bag with the wet sample was reweighed again.

The percentage absorption (water uptake) was calculated using the relation

$$\text{Absorption/water uptake (\%)} = (w_2 - w_1/w_0) \times 100$$

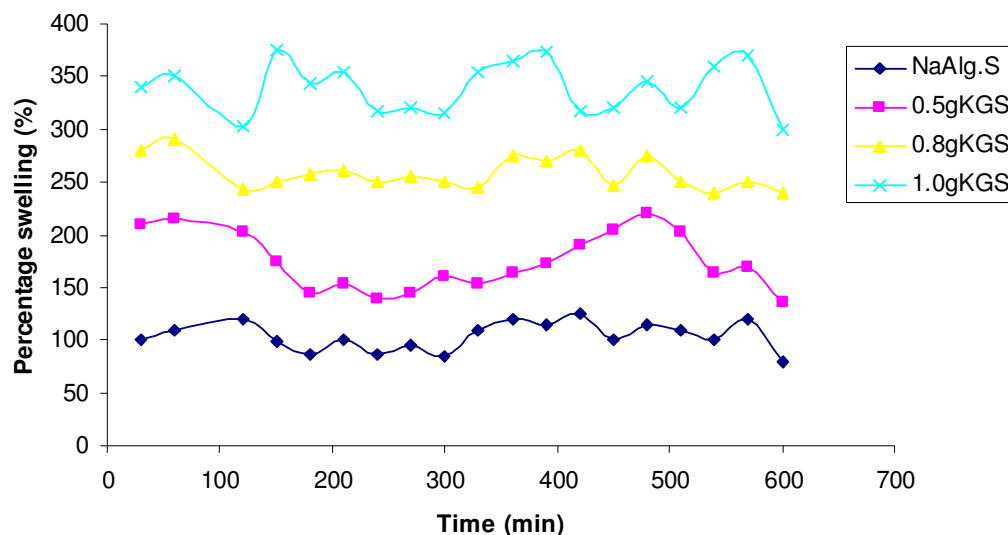
Where:  $w_2$  = weight of the wet bag plus sample

$w_1$  = weight of the dry bag plus sample

$w_0$  = weight of the original sample

#### Drug Release Measurement

The release of the drug was carried out by a standard method described by Baljit *et al.*, 2007b. That is, the release of the drug was carried out by placing dried and loaded sample in definite volume of the releasing medium at 27°C. The amount of



**Figure 1.-Effect of concentration of galactomannan on swelling of hydrogels**

indomethacin released was measured by standard acid base titration method. The drug release was measured after fixed interval of time and release dynamics of the model drug was calculated.

## RESULTS AND DISCUSSION

### Effect of Galactomannan Concentration on Swelling

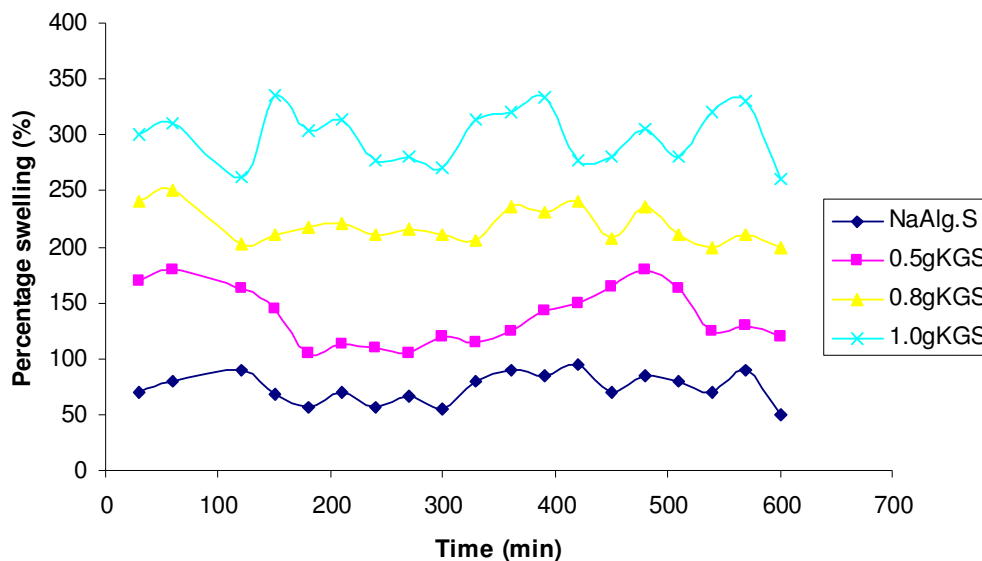
The chemical structure of the polymer affects the swelling ratio of the hydrogels which is directly related to loading of drug to the polymers and release of drug from the polymeric matrix. The chemical structure depended upon composition of the polymeric matrix i.e the crosslinking ratio. The higher the crosslinking ratio, the more crosslinking agent is incorporated in the hydrogels structure. Highly crosslinking hydrogels have a tighter structure, and will swell less compared to the same hydrogels with lower crosslinking ratios. Crosslinking hinders the mobility of the polymer chain, hence lowering the swelling ratio. Swelling of environmentally-sensitive hydrogels can be affected by specific stimuli. In the hydrogels systems, absorption of water from the environment changes the system and thus the drug release kinetics (Baljit et al., 2007a).

The effect of galatomanan concentration on swelling at room temperature (27°C) is presented in Figure 1. From the Figure 1, it can be seen that there is an irregular increase and decrease which final decreases at the tenth hour. This undulation of swelling signifies a loose in network structure that imbibes water molecules more than its network structure could hold. This leads to bursting of the structure and of the cycle of hydration. Similar report was reported by Alice and Alokray 2002.

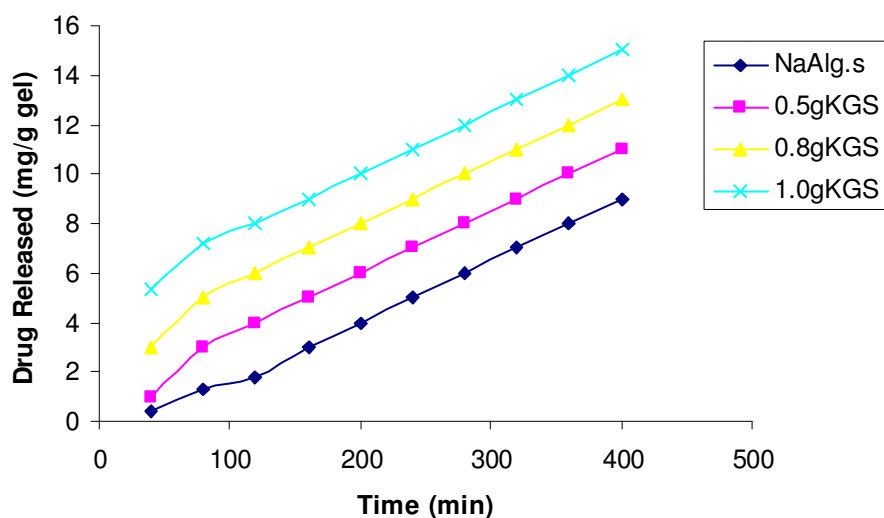
Addition of 0.5gKGS, gave a very sharp increase in swelling. This shows that addition of galactomannan increases the hydrophilicity and porosity of the hydrogel, which lead to more penetration of water. However clogging of the pores due to the rapid hydration sticking the three-dimensional structure, result in decrease in swelling with increase in time. These results confirmed the initial burst effect obtained in many alginate network structure as reported by El-kamel *et al.*, (2002). For an increase concentration of 0.8gKGS, the network structure becomes less rigid thereby leading to more hydration rate as such; the percentage swelling attained its maximum at 480 minutes. Further addition of 1.0gKGS leads to high water uptake. This is due to increase in porosity and hydrophilicity of the hydrogel as result of addition of more galactomannan (Alice and Alokray, 2002). These results indicate that the hydrogels absorbed reasonable amount of water without dissolution which is one of the most important properties of hydrogels for use in drug delivery.

### Effect of Indomethacin on Swelling of Hydrogels

The effect of drug (indomethacin) on swelling of the hydrogels is presented in Figure 2. The percentage swelling of the hydrogels behaves the same as in Figure 1. That is increasing and decreasing and finally dropped at the tenth hour. Also the percentage swelling increases with increase in the concentration of galactomannan. This is due to increase in porosity and hydrophilicity of the hydrogels as a result of increase in concentration of the galactomannan. The effect of drug on swelling of hydrogels is shown in the water uptake. That is the rate of water uptake of hydrogels in Figure 2 is less compared to those in Figure 1. This is due to the fact that the drug



**Figure 2.** Effect of indomethacin on swelling of hydrogels



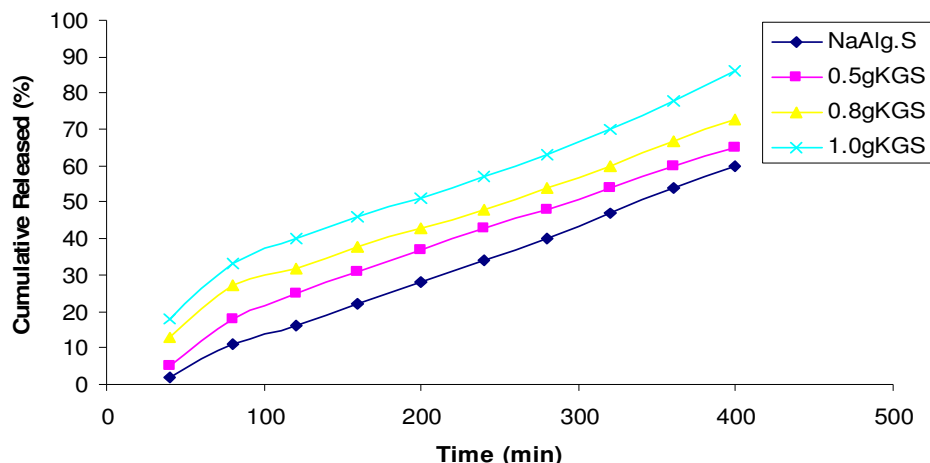
**Figure 3.** Release of indomethacin from drug loaded sample of KGS hydrogels in 25ML of distilled water at 25°C

might have penetrated into the hydrogels and blocked pores in the network structure. Similar report has been reported by Alice and Alokraj, 2002.

### Drug Delivery Behaviour

The release of water-soluble drugs, entrapped in hydrogels, occur only after water penetrates the polymeric networks to swell and dissolve the drug,

followed by diffusion along the aqueous pathways to the surface of the devices. The release of the drug is closely related to the swelling characteristics of the hydrogels, which in turn, is a key function of the chemical architecture of the hydrogels (Baljit et al., 2007a; 2007b). The release profile of indomethacin from per grams of the drug loaded hydrogels is presented in Figure 3 and 4. The amount of drug released was higher in 1.0gKGS and the lowest was that of NaAlg.S. This observation is also supported from the Figure of percentage cumulative



**Figure 4.** Percentage of cumulation released of indomethacin from drug loaded sample in distilled water

release (Figure 4). From the percentage cumulative release of indomethacin, it was observed that 50% of the total release for 1.0gKGS occurred at 180 minutes (Figure 4), whereas 50% of the total release of the drug for NaAlg.S, 0.5gKGS, and 0.8gKGS occurred at 100, 130, and 145 minutes respectively (Figure 4). From these result it is clearly indicated that the hydrogels have potentials for drug release but 1.0gKGS offer best release.

## CONCLUSION

The hydrogels absorbed and retained reasonable amount of water without dissolution, which is affected by composition of the KSG. This is one of the most important properties of hydrogels for use in drug delivery. The hydrogels also have potentials to release drug but hydrogels prepared with 0.8gKGS and 1.0gKGS offers better release behaviour of the drug model. It can be concluded that the hydrogels prepared from KGS have potentials to use in drug delivery devices in addition to the existing one. The following recommendations will be important for further research in these areas of studies:-

- The viscosity measurement of the galactomannan hydrogels and investigation into the effect of cross linking of the polysaccharide on the release of konkoli (*maesopsis eminii*)
- Study of the drug loading, ionic strength, pH measurement and other process parameters on drug release will be require to produce matrix Tablets with desired release rates.

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