ENCAPSULATION OF *Moringa oleifera* LEAVES WITH GALACTOMANNAN HYDROGEL SYSTEMS FOR POTENTIAL APPLICATION IN DIABETIC DRUGS

Supported by tetfund

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Received: July 19, 2020 **Accepted:** October 18, 2020

Abstract: A novel hydrogel systems were formulated using konkoli (*Maesopsiseminii*) galactomannan, borax as cross linking agent to encapsulate leaves powder and aqueous extracts of leaves of *Moringa oleifera (M. oleifera)*. Glucose responses of the encapsulated products were carried out by swelling studies. The swelling behavior of the hydrogels showed increase in swelling with increase in time. The swelling was highly dependent on the amount galactomannan in the formulation. Water absorbed affect the structure of the cross linked hydrogels and hence the release of the *M. oleifera* matrix, the swelling pattern exhibited by the hydrogels in distilled water was maintained in 10% glucose solution. At this high glucose concentration, the hydrogels showed distinct rapid swelling within 5 – 6 h with maximum swelling value above this period. The results obtained in this study shows that the hydrogel systems could act as insulin mimetics for the treatment of diabetics.

Keywords: Diabetics, encapsulation, hydrogel, galactomannan, *Moringa oleifera*

Introduction

The use of Herb is staging a comeback and herbal revival is happening all over the globe. The herbal products today symbolize safety in contrast to the synthetic products that are regarded as unsafe to humans and environment (Joy *et al*., 1998). Although herbs had been priced for medicinal, flavoring and aromatic qualities for centuries, the synthetic products of modern times have surpassed their importance for a while. However the blind dependence on syntheticproducts is over and people are returning to naturals with the hope of safety and security (Joy *et al*., 1998).

In many of the developing countries, the use of plant drugs is increasing because modern lives saving drugs are beyond the reach of many citizens. Plants synthesize and preserve a variety of biochemical products, many of which are extractable, used as chemical feed stocks, raw materials for various pharmaceutical products or scientific investigations. In some cases, the crude extract of medicinal plants may be on the other hand, the isolation and identification of the active principles and elucidation of the mechanism of the action of a drug is of paramount importance (Joy *et al*., 1998).

Zogale (*M. oleifera)* tree is well known in India and cultivated in all tropical and sub-tropical areas of the world (Isabella *et al*., 2003). It is commonly known as miracle tree because all its parts (leaves, flowers, stem-bark, roots, seeds) are used especially for their pharmacological and nutritional properties *M. oleifera* seeds are rich in protein and oil (Behen oil) has been well known and was traditionally used in medicine, for beauty care and preparation of religious ointment. It has also been used as lubricants by watch makers. *M. oleifera* seeds are also used in tropical regions for water purification. Recently, the leaves, seeds and other parts of *M.* oleifera are used in folk medicine in India. At present the leaves are only eaten as vegetable, the seeds, bark are used as anti-cancer (Isabella *et al*., 2003).

Diabetes mellitus is a set of related diseases in which the body cannot regulate the amount of sugar specifically glucose in the blood. Glucose in the blood gives us energy to perform daily activities, from the foods we eat; glucose in the bloods is produced by the liver. In a healthy person, the blood glucose level regulated by several hormones, including insulin, insulin is produced by the pancreas, a small organ between stomach and liver. Insulin allows glucose to move from the blood into the liver, muscle, and fat cells, where it is used for fuel.

Hydrogels are unique class of polymeric materials which take in a significant amount of water into internal molecular structure and maintain their original shape. The dried Hydrogels (Xerogels) when in contact with a thermodynamically compatible solvent, they undergo a glassy to rubbery transition (Onyiriha, 2005) and this property accounts for a great number of applications in bio-medical and pharmaceutical fields (Peppas *et al*.,, 2000). Recently some prominent applications of Hydrogels include: Controlled delivery systems, replacement of blood vessel, wound dressing and soft contact lenses (Rosiak *et al*., 1995).

This paper reports the development of less expensive antidiabetic drug and glucose biosensors from *M. oleifera* leaves. The hydrogel systems containing *M. oleifera* matrix could be used as less expensive treatment of diabetes. The systems may also be used as glucose biosensors and may serve as alternatives for insulin delivery systems.

Materials and Methods

Plant collection and preparation

Fresh leaves of M. oleifera (Zogale) and *Maesopsiseminii* (Konkoli) seeds were obtained from Demsa local Government area of Adamawa state, Nigeria. *Konkoli gum* seeds were pounded and sieved to get a fine raw *Konkoli gum seeds* powder. Air – dried *M. oleifera* leaves were grounded to powder. Water extracts were obtained by extraction with distilled water (10 g per 100 ml) and boiling for 2 h. The solution was cooled and filtered using filter paper. The residue was re-extracted twice using (100 ml) distilled water. The filtrate was further filtered using sintered glass, and a clear filtrate obtained (Wang *et al.,* 2010).

Immobilization of leave powder onto hydrogel systems

A 25 ml portion of distilled water was transferred into 250 ml glass beaker, 6.5 g of konkoli gum powder was added, then 0.5 g of *M. oleifera* leave powder was transferred into same beaker, mixed thoroughly to form a viscous solution. Then 2.6 g of borax was added to this solution and stirred with a glass rod to form a gel. The gel was cast on a clean polyethylene surface and allowed to dry over a period of 72 h (John, 2005).

Repeating the procedure above, different hydrogel matrices were formed using 6.0, 5.5, 5.0, 4.5 and 4.0 g of konkoli gum powder with 1.0, 1.5, 2.0, 2.5 and 3.0 g of *M. oleifera* leave powder with 2.6 g of borax were used to form another set of hydrogels matrices. The different hydrogel matrices formed were designated with letters A, B, C, D, E and F, in ratio of Kg/Ml/borax ratio.

Encapsulation of M. oleifera leaves extracts

The method previously described by John (2005) was followed: A 25 ml of the extracts obtained from leaves powder was transferred into a glass beaker; 6.0 g of konkoli

gum powder was added and mixed thoroughly to form a viscous solution. Then 2.6 g of borax was added to this solution and stirred with a glass rod to form a gel. The gel was casted on a clean polyethylene surface and allowed to dry over a period of 72 h.

Swelling measurement

Dynamic method was used in this measurement (Osemeahon, 2003). This is a modified "tea bag" that involves: instead of a Nylon mesh screen, a transparent polyethylene bags were used here and instead of hanging the bags to drain off the water solution a micro syringe was used to suck away the excess solution. The modified "tea bag" method entailed immersion of dried hydrogel in distilled water (10 ml) inside a polyethylene bag (pre-weighed with mouth sealed). The bag with its contents was then left undisturbed and monitored within a period of 1 – 10 h at room temperature (25 – 30^{0}C) at different time interval excess solution was carefully sucked out. The bag with the wet sample was reweighed to obtain weight of sample after swelling;

Absorption (%) = ((Ws-Wd)/Wg) x 100

Where: Wd = Weight of dry sample plus bag, Ws = Weight of Wet sample plus bag, Wg = Weight of original sample

Results and Discussion

The drying processes for prepared hydrogel membrane containing the encapsulated products differ due to the amount of both *M. oleifera* leave powder and galactomannan. The drying period for hydrogels containing high concentrations of *M. oleifera* products was 48 h but the membranes were lighter. However, it was observed that the higher the amount of galactomannan, the thicker the membrane and the longer the drying period (72 h was recorded).

Experiments were conducted to exploit the hydrogel membranes as candidates for oral formulations containing mixtures of the hydrogels with varying amount of *M. oleifera* materials for pharmaceutical applications. The first step to achieve this was to assess the leaching of these materials from the membranes using swelling measurements.

Swelling is an important parameter to be studied in this work. It helps in explaining the interaction of the matrix with glucose and will give an insight on how the matrix will respond to glucose levels and perhaps induce insulin sensitivity in a diabetic patient

From Fig. 1, the swelling ratio increased with increase in time. The swelling was highly dependent on the amount of galactomannan in the formulations. It was observed that the higher the amount of galactomannan in the hydrogels, the lower the swelling ratios. Hence, the swelling order of the hydrogel systems containing *M. oleifera* leaves powder was A<B<C<D<F

For membrane systems A and B with high concentration of galactomannan, the swelling increased gradually with time up to 7 h and decreased thereafter. The possible reason for this is that the swelling in aqueous media strongly depends on the extent of effective crosslink density provided by the borax since this density will increase with the increase of the galactomannan polymer chain concentration. The hydrogels C, D and F showed higher swelling with initially rapid swelling rate up to 3 h. This rate dramatically increased between 3 – 6 h and 6 – 7 h. However, the rate slightly deceased after 7 h. The rapid swelling may be due to porosity of the hydrogel structures and low crosslink density of the hydrogel as a result of the high amount of the *M. oleifera* matrix as well as possible increase in the osmotic pressure inside the hydrogels. Above 7 h the hydrogels may start disintegrating (or dissociate) which will account for the slight decrease in swelling ratio observed.

From the swelling behavior, it is imperative to state that rate of water absorption may affect the structure of the cross-linked hydrogels and hence the rate of release of the incorporated *M. oleifera* matrix. This is because the amount of water that penetrates into the membranes, and the rate of this penetration are critical to the dissolution of the immobilized material. Depending on the solubility of material, it will dissolve and finally diffuses out of the membrane into solution at regulated intervals. Considering the large amount of water absorbed by all the hydrogels, they may be recommended as suitable for bio-adhesive delivery of water-soluble drugs.

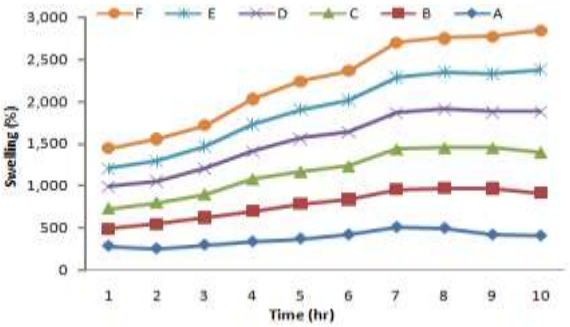

Fig. 1: Effect of increasing amount of *M. oleifera* leaf powder on swelling of hydrogel systems

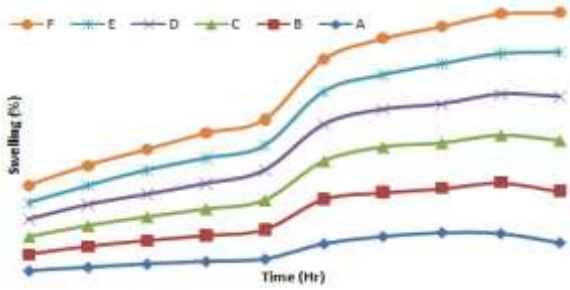

Fig. 2: Swelling of hydrogels containing leaf powder in 10% glucose solution

Swelling properties of immobilized leaf powder

Glucose sensitive hydrogels are sugar sensitive and show variability in response to the presence of glucose. Fig. 2 shows the swelling behavior of hydrogels containing leaves powder in 10% glucose solution. For the leaves powder systems, the swelling pattern exhibited by the hydrogels in distilled water is still maintained in 10% glucose solution. At this high glucose concentration, the hydrogels showed distinct rapid swelling within 5 – 6 h with maximum swelling values above this period.

The pattern exhibited by C, D and F hydrogels with leaves powder showed high swelling rates within 1 – 4 h with maximum values above this period. But hydrogels A and B exhibited slightly swelling rates above 4 h and had low swelling values compared to hydrogels C, D and F.

Under a glucose environment, the glucose diffuses into the hydrogel, and could be converted to gluconic acid that may be accompanied with an increase in pH. As a result there could be an increase in the swelling ratio (Traitel *et al*., 2000; Odee, 1998; Pluta and Karawicz, 2004; Eddigton and Beebe, 2004) as shown in Figs. 1 – 4. Hence, the swelling of the hydrogel may lead to the liberation of the *M. oleifera* material which controls the glucose level in the blood. The release devices formulated in this work may act as insulin mimetic for possible use in ameliorating diabetes status. For the design self-regulating *M. oleifera* delivery devices for the management of diabetes, the changes occurring in the proposed hydrogel systems in response to glucose need to be

appropriate for diabetic physiological glucose levels. Also, the morphology of the hydrogels should be able to control the diffusion of *M. oleifera* products in a regulated manner. Therefore the hydrogels must be highly cross-linked as to prevent the relevant degree of relaxation required to produce a change in state upon glucose triggering. Hydrogels A and B containing leaves powder and seed paste could be recommended for such devices.

For most individuals, the upper normal limit of fasting plasma glucose is 6.4 mmol/L (115 mg/dL. Diabetes is reliably diagnosed when fasting plasma glucose concentrations are 47.8 mmol/L (140 mg/dL). Alternatively, a 2 h postprandial plasma glucose concentration of 11 mmol/L (200 mg/dL) may be indicative of diabetes. Therefore, for a self-regulating *M. oleifera* delivery device to work effectively, it needs to begin to deliver its therapeutic agents at concentrations above 6.4 mmol/L. Glucose concentrations of 5% and 10% were used to test the sensitivity of the formulated hydrogel systems as explained earlier.

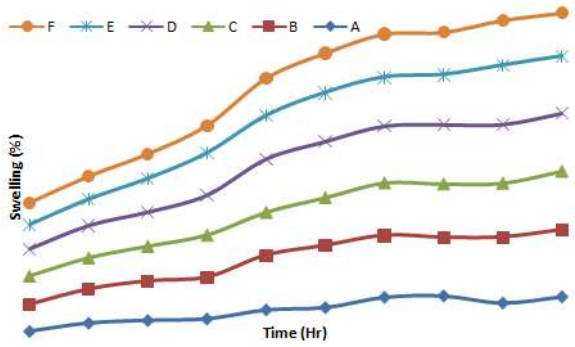

Fig. 4: Swelling of hydrogels containing leaf powder in 5% glucose solution

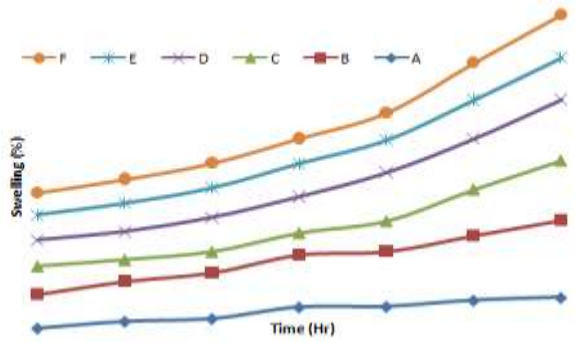

Fig. 3: showing the swelling behavior of hydrogels containing leaves powder in 5% glucose solution

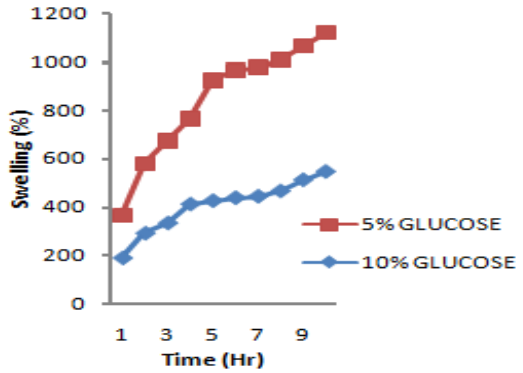

Fig. 5: Swelling behaviour of aqueous extracts of encapsulated *moringa* leaves in glucose solutions

In Fig. 5, the hydrogel devices containing aqueous extracts of leaves and seeds show a large decrease in swelling behavior in response to an increase in glucose concentration from 5 to 10%. Hence there is a possibility of high swelling rates within a physiological 0.1–1% glucose level (which is an upper glucose limit of 55 mmol/L in diabetics). Perhaps, the rise in swelling ratio at lower glucose concentration ranges would be acceptable for use in a device similar to insulin delivery systems.

In our research work, new hydrocolloid from *konkoli* seed gum was cross-linked with borax and used in the encapsulation of leaf powder and aqueous extracts of leave. Hence, different hydrogel systems were formulated from these materials and assessed for glucose response in solution using swelling measurement.

The swelling behavior of the hydrogel systems in distilled water showed that swelling increases with increase in time. The swelling behavior is highly depends on the amount of galactomannan in the formulation, the higher the amount of galactomannan in the hydrogel the lower the swelling ratio. Considering the large amount of water absorbed by all the hydrogels, they may be recommended as suitable materials for bio adhesive delivery of water soluble drugs. Specifically, this work shows that the hydrogel systems could act as insulin mimetic for management of diabetics.

Conclusion

In conclusion less expensive hydrogel systems were formulated for use as drug delivery systems which could acts as insulin mimetics for treatment of diabetes.

Conflict of Interest

Authors have declared that there is no conflict of interest reported in this work.

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