RSC Advances

ROYAL SOCIETY OF CHEMISTRY

www.rsc.org/advances

Polysaccharide based superabsorbent hydrogel from *Mimosa Pudica*: Swelling-deswelling and drug release

Gulzar Muhammad,[a] Muhammad Ajaz Hussain,*[a] Muhammad Umer Ashraf,[b] Muhammad Tahir Haseeb,[b] Syed Zajif Hussain[c] and Irshad Hussain[c]

[a]*Department of Chemistry, University of Sargodha, Sargodha 40100, Pakistan.* majaz172@yahoo.com

[b]*Faculty of Pharmacy, RH Tariq Block, University of Sargodha, Sargodha 40100, Pakistan*

[c]*Department of Chemistry, SBA School of Science & Engineering (SSE), Lahore University of Management Sciences (LUMS), DHA, Lahore Cantt 54792, Pakistan*

Herein, we have evaluated a polysaccharide, glucuronoxylan isolated from seeds of *Mimosa pudica* (MP) for its water holding capacity, pH and salt responsive swelling-deswelling, and sustained drug release. MP hydrogel (MPH) has shown high water retention capacity. MPH exhibited negligible swelling at pH 1.2 while high swelling was observed at pH 6.8, 7.4 and in deionized water which followed second order kinetics. Whereas, MPH deswells in NaCl and KCl solutions and ethanol. The presence of interconnected macropores with an average diameter of 62.94 μm was revealed by scanning electron microscopy (SEM) of swollen then freeze dried sample of MPH. Furthermore, MPH was explored as a sustained release material for tablet formulation of diclofenac sodium. Drug release mechanism from MPH containing tablet formulation was found super case-II transport. Results have indicated that MPH could be a potential candidate for sustained release formulations.

1 Introduction

Mimosa pudica L. (Syn: chui mui, lajwanti, touch me not, sensitive plant, shy plant and sleepy plant) is a sensitive diffused shrub of family *Mimosaceae* widely distributed in Tanzania, Brazil, America, Asia, Nigeria and many Pacific islands. The plant is rich in alkaloids, sterols, terpenoids, tannins and flavonoids[1-4] and has been used to treat ulcers, piles, respiratory troubles, constipation, malaria, snake bites, depression, small pox, dysentery, pyrexia, inflammations, etc.[5-8] MP seeds extrude hydrogel when soaked in water. The main component of this extruded hydrogel is glucuronoxylan (GX) and is composed of D-xylose and D-glucuronic acid.[9,10]

Hydrogels are water swellable polymers that retain large amount of water depending upon the presence of hydrophilic functional groups (-OH, -COOH, -$CONH_2$), flexibility of network,

level of crosslinking and porosity of polymer.[11] Hydrogels are appropriate candidates for applications in cosmetics, agriculture, pharmaceuticals, horticulture, engineering, sustained drug release, enzyme immobilization and disposable diapers because of their bioavailability, biocompatibility, biodegradability and non-toxic nature.[12-15] These smart materials are responsive to temperature, pH, ionic strength and electric field.[16-20] The pH sensitivity of these intelligent hydrogels makes them suitable for controlled and sustained release of drugs.[21-23] These properties are due to the presence of aforesaid functional groups that are present on polymer chain.[24,25]

Herein, we introduced a novel superabsorbent, superporous and smart polysaccharide, GX isolated from MP seeds for sustained drug release. The present study was focused on the water holding capacity, swelling kinetics, pH and salt responsive properties of MPH. We also reported on swelling-deswelling (on-off switching) properties of MPH against different stimuli. These attributes of MPH have not been discovered yet. We also used simulated gastric fluid (SGF) and simulated intestinal fluid (SIF) to evaluate MPH as a sustained release material for diclofenac sodium formulations. We were also interested to see the morphology of MPH, its tablet formulation and swollen then freeze dried MPH.

2 Materials and methods

2.1 Materials

Seeds of MP were purchased from local market. Potassium dihydrogen phosphate, *n*-hexane, ethanol, potassium chloride, sodium chloride and hydrochloric acid were purchased from Riedel-de-Haën, Germany. Analytical grade sodium hydroxide (Merck) was standardized with oxalic acid before further use. Deionized water was used throughout the study. SGF and SIF were

prepared according to method given in United States Pharmacopeia (2010). Polyvinylpyrrolidone (PVP K30), magnesium stearate, diclophenac sodium (DS) and microcrystalline cellulose were purchased from Fluka.

2.2 Methods

2.2.1 Isolation of hydrogel. Clean seeds of MP were soaked in water for 12 h and then warmed at 50 °C for 30 min. Seeds extruded hydrogel which was separated by cotton cloth. Extracted hydrogel was washed with *n*-hexane to remove lipophilic substances and then dried at 50 °C in a vacuum oven. Dried hydrogel was kept in vacuum desiccator after grinding and passing through 60 mesh sieve.

2.2.2 Flow-ability parameters of MPH.

2.2.2.1 Angle of repose. Angle of repose was determined by fixed funnel method in order to study the flowability of hydrogel.[26] Powdered hydrogel was allowed to fall through fixed funnel on a graph paper. Angle of repose (θ) was determined by calculating the height (*h*) and radius (*r*) of heap by the following eqn (1);

$$\mathrm{Tan}\,\theta = \frac{h}{r} \qquad (1)$$

2.2.2.2 Bulk and tap density. Volume of hydrogel (V_b) was recorded by placing hydrogel (1.0 g) in graduated cylinder. Tapped volume (V_t) was noted after tapping graduated cylinder 100 times. Bulk density (D_b) and tap density (D_t) were calculated by eqn (2) and (3) respectively;

$$D_b = \frac{Weight\ of\ hydrogel}{Volume\ of\ hydrogel\ (V_b)} \qquad (2)$$

$$D_t = \frac{Weight\ of\ hydrogel}{Tapped\ volume\ (V_t)} \quad (3)$$

2.2.2.3 Hausner ratio and Carr's index. Hausner ratio and Carr's index are frequently employed to study flow properties of hydrogels.[26] Hausner ratio is the ratio of tap density to bulk density given by the eqn (4);

$$Hausner\ ratio(H) = \frac{D_t}{D_b} \quad (4)$$

whereas, Carr's index is the percentage ratio representing arrangement of particles and is calculated by the eqn (5);

$$Carr's\ index(C) = 100 \times \left(1 - \frac{D_b}{D_t}\right) \quad (5)$$

where D_b and D_t are bulk and tap densities, respectively.

2.2.2.4 Moisture content. Sartorius Thermo Control Infrared Dryer (YTC 01L, Germany) was used to determine moisture content of MPH. Weight of hydrogel was recorded before and after drying at 105 °C for 1 h.

2.2.3 Centrifuge retention capacity. Water retention capacity or centrifuge retention capacity was assessed by centrifuging freshly prepared solution of hydrogel (1% w/w) in deionized water at 4500 rpm for 30 min at room temperature. Supernatant was decanted and weight of wet sediment paste was noted. This wet sediment paste was completely dried at 70 °C and weight of the dried mass was noted. Water retention capacity is the ratio of wet sediment mass to dried mass.[27,28]

2.2.4 Swelling capacity. Tapped volume of powdered hydrogel (1.0 g) was noted by placing it in a graduated cylinder and tapping it 100 times. Then hydrogel was mixed in deionized water thoroughly and the volume was adjusted to 100 cm^3. Sediment volume of swollen hydrogel was observed after keeping for 24 h and swelling capacity (*v/v*) was calculated as ratio of swollen to tapped volume.

$$Swelling\ capacity\ (v/v) = \frac{Swollen\ volume}{Tapped\ volume} \quad (6)$$

2.2.5 Dynamic and equilibrium swelling. To find out pH dependent swelling, MPH (0.5 g) was packed in cellophane bags and soaked in hydrochloric acid buffer (pH 1.2), phosphate buffers (pH 6.8 and 7.4) and deionized water for 24 h. The pH values were calibrated precisely using pH meter (JENWAY 3510, UK). Weight of swollen hydrogel was noted after regular intervals for 24 h and swelling capacity (g/g) in each case was calculated as;

$$Swelling\ capacity\ (g/g) = \frac{W_t - W_0 - W_c}{W_0} \quad (7)$$

where, W_t is the weight of swollen hydrogel with wet cellophane bag, W_0 is the weight of dry hydrogel and W_c is weight of wet cellophane bag.

The normalized degree of swelling, Q_t is the ratio of media (buffers of pH 1.2, 6.8, 7.4 and deionized water) penetrated into gel to initial weight of hydrogel at time *t* and can be calculated using eqn (8).

$$Q_t = \frac{W_s - W_d}{W_d} = \frac{W_t}{W_d} \quad (8)$$

where, W_s is the weight of swollen hydrogel at time *t*, W_d is the weight of dried hydrogel at time t=0 and W_t is the weight of water penetrated into hydrogel at time *t*.

Normalized equilibrium degree of swelling (Q_e) is the ratio of media penetrated into hydrogel at t_∞ to weight of dried hydrogel at t=0. It can be determined using eqn (9);

$$Q_e = \frac{W_\infty - W_d}{W_d} = \frac{W_e}{W_d} \quad (9)$$

where, W_∞ is the weight of swollen hydrogel at time t_∞ when swelling remains constant, W_d is the weight of dried hydrogel at t=0 and W_e is the amount of water absorbed by hydrogel at t_∞.

2.2.6 Swelling kinetics. Normalized degree of swelling (Q_t) and normalized equilibrium degree of swelling (Q_e) values can be used to find the kinetic order of swelling.[29] For second order kinetics, eqn (10) was used.[30]

$$\frac{t}{Q_t} = \frac{1}{KQ_e^2} + \frac{t}{Q_e} \quad (10)$$

The plot between $\frac{t}{Q_t}$ on y-axis and t on x-axis should be a linear line with slope of $\frac{1}{Q_e}$ and intercept of $\frac{1}{KQ_e^2}$.

2.2.7 Swelling in salt solutions. Swelling behavior of MPH was recorded by soaking hydrogel containing cellophane bags in 0.1, 0.2, 0.3, 0.4, 0.5, 1.0, 1.5 and 2.0 M solutions of NaCl and KCl at 25 °C and equilibrium swelling was recorded after 24 h using eqn (7).

2.2.8 Swelling-deswelling behavior in response to external stimuli. Gravimetric method was employed to monitor swelling and deswelling of MPH. The hydrogel was allowed to swell in deionized water for 1 h and then immersed in pure ethanol to measure its weight as a function of deswelling time of 1 h.

In another experiment, swelling-deswelling behaviour was studied using buffer solutions (pH 7.4 and 1.2). Hydrogel was kept in pH 7.4 buffer for 1 h to determine its swelling and then allowed to deswell for 1 h in buffer solution (pH 1.2). Similarly, swelling-deswelling was studied in water and aqueous NaCl solution (0.9%). These on-off experiments were performed for four times. All experiments were repeated three times and mean values were reported.

2.2.9 Scanning electron microscopy (SEM). The surface morphology and internal structure of MPH were analyzed by scanning electron microscope (FEI Nova, NanoSEM 450) operating at 10 kV, equipped with a low energy Everhart-Thornley detector (ETD) using secondary electrons. For this purpose, dried hydrogel (0.1 g) was mixed in deionized water (2 mL) with mixer mill and further sonicated (30 min) to remove air bubbles. The swollen MPH was frozen at -20 °C and then freeze-dried. Afterwards, the transverse and vertical cross-sections of hydrogel were obtained using sharp blade to reveal its porous nature. The obtained cross-sections were mounted on aluminum stub with silver paint and further coated with gold using sputter coater (Denton, Desk V HP) operating at 40 mA for 30 s under vacuum and analyzed with SEM. SEM analysis was also recorded for air dried MPH and surface of tablet.

2.2.10 Preparation of tablets. Wet granulation method was employed to prepare tablets of DS. For this purpose, MPH, DS and microcrystalline cellulose were passed through 40-mesh sieve, thoroughly homogenized with pestle and mortar, and granulated with solution of polyvinylpyrrolidone (PVP K30) in isopropyl alcohol. The resultant wet mass was passed through 20-mesh sieve after drying at 40 °C and then lubricated with magnesium stearate. Rotary tablet press fitted with 11 mm punch was used to prepare the tablet (350 ± 5 mg). The manufactured tablets were studied for their hardness, thickness and friability which were found in the range of 6-7 kg/cm^2, 4.15-4.19 mm and 0.82-0.96%, respectively. Later on, tablets were

evaluated to study the effect of MPH on the release behavior of DS. Table 1 shows the composition of different formulations of MPH.

Table 1 Composition of oral tablet formulations of DS based on MPH

Formulation composition (mg/tablet)	F1	F2	F3
MPH	100	150	200
DS	100	100	100
Microcrystalline cellulose	125	75	25
PVP K30	20	20	20
Magnesium stearate	5	5	5

2.2.11 ***In-vitro*** **drug release study.** The effect of MPH on the release of DS tablets was studied in SGF (900 mL, pH 1.2) for 2 h using USP Dissolution Apparatus II. The tablets were then shifted to SIF (900 mL, pH 7.4) and release behaviour was studied for 14 h at 37 °C and 50 rpm. After fixed time intervals, from SGF and SIF media, sample (5 mL) was withdrawn, filtered, diluted (if necessary) and analyzed through UV/Vis spectrophotometer (Shimadzu, Japan) at 276 nm. Fresh SGF or SIF was added to make up withdrawn volume. The experiment was performed in triplicate and cumulative percentage of drug release was expressed as mean values. The results of MPH containing formulations were compared with a commercial formulation of DS (Voltral® SR 100 tablet).

The drug release from water-swellable polymers is mainly controlled by diffusion mechanism which can be better explained by power law equation (eqn 11)[31] as follows;

$$\frac{M_t}{M_\infty} = k_p t^n \quad (11)$$

where, M_t/M_∞ is the fraction of drug released in time t, k_p is the power law constant and n is the diffusion exponent.

The drug release mechanism corresponds to the value of this diffusion coefficient (n). The drug release from hydrogel follows Fickian diffusion mechanism if the value of n is 0.45. The mechanism will be non-Fickian diffusion (controlled by both swelling and diffusion) when the value of n ranges between 0.45 and 0.89. If value of n is greater than 0.89, the mechanism is super case-II transport in which rate remains constant for longer periods of time and shows exponential increase in drug release at the end due to matrix erosion.[32,33]

3 Results and discussion

3.1 Physical properties of MPH

Carr's index, Hausner ratio and angle of repose indicated that powder MPH had poor flow-ability. The physical properties of hydrogel are given in Table 2.

Table 2 Physical properties of MPH

Physical properties	MPH

Moisture content (%)	12 ± 0.20
Average particle size (μm)	≈259
Angle of repose	46 ± 0.25
Bulk density (g/cm^3)	0.2 ± 0.01
Tapped density (g/cm^3)	0.363 ± 0.01
Carr's index (%)	44.1 ±1.50
Hausner ratio	1.82 ± 0.06
Swelling capacity on 24 h (g/g)	55.42 ±2.00
Centrifuge retention capacity (%)	87.28 ± 1.11

3.2 pH responsive swelling of MPH

Swelling behavior of MPH was evaluated in buffers of pH 1.2, 6.8 and 7.4, mimicking the pH values of stomach, small intestine and large intestine, respectively (Fig. 1a). It was observed that swelling in acidic buffer (pH 1.2) is markedly less than swelling in basic buffers and deionized water. This is mainly due to the protonation of carboxylic acid groups present on the polymer chains. Increase in pH increases the ionization of carboxylic acid groups that resulted in anion-anion repulsions hence enhances the swelling in alkaline media. Moreover, swelling capacity was found low in basic buffers as compared to deionized water. This low swelling capacity in alkaline media may be due to charge screening effect of excess cations that put a stop to anion-anion repulsions due to shielding of carboxylate anions. Literature revealed that many other hydrogels showed pH dependent water absorbency.[34,35] Therefore, based on pH dependent swelling of MPH, it can be said that MPH is potential candidate for drug release formulations.

3.3 Swelling kinetics

Swelling of hydrogel is controlled by diffusion of solvent and relaxation of polymer chain as explained by 2nd order kinetic model.[36] The kinetic studies were performed on swelling data of MPH obtained in water and at pH 6.8 and 7.4. Fig.1b shows a plot of t/Q_t *vs* t which is linear with a slope of $1/Q_e$ and an intercept of $1/kQ_e^2$ indicating best fit of swelling data to 2nd order kinetic model.

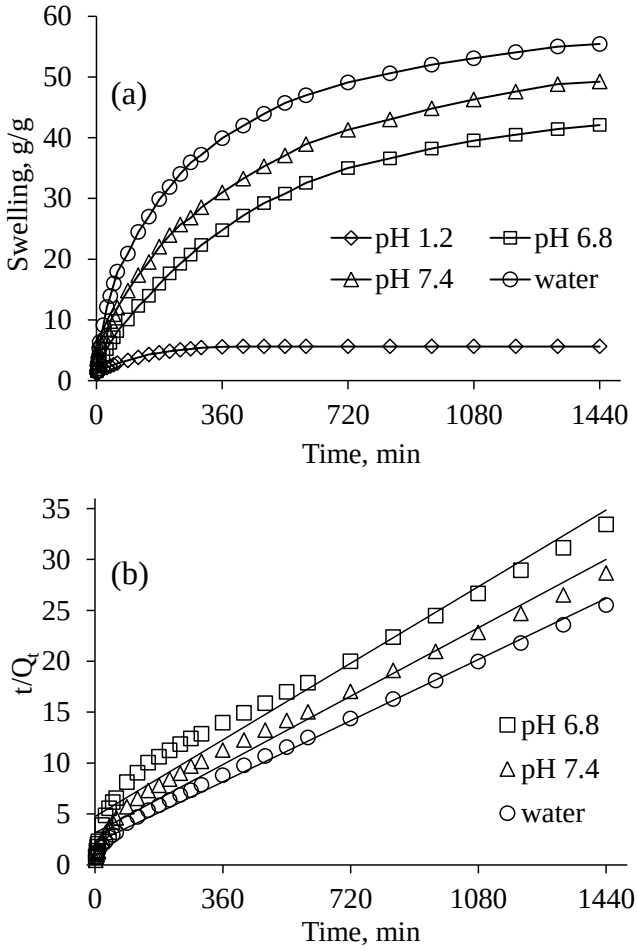


Fig. 1 (a) Swelling capacity and (b) swelling kinetics of MPH in deionized water and different buffers.

3.4 Saline responsive swelling of MPH

Swelling of hydrogels mainly depends upon salt concentration and charge on ions along with nature of polymer, i.e., presence of hydrophilic groups and elasticity of network, etc.[37] It was found that swelling capacity of MPH decreases abruptly with increase in concentration of salts (Fig. 2). This reduced swelling in salt solutions might be due to charge screening effect of excess cations resulting in non-perfect anion-anion electrostatic repulsions.[38] Smaller ions with greater charge density interact more strongly with carboxylate anions and decrease anion-anion repulsions.[39] Therefore, MPH deswells more in NaCl solution as compared to KCl solution.

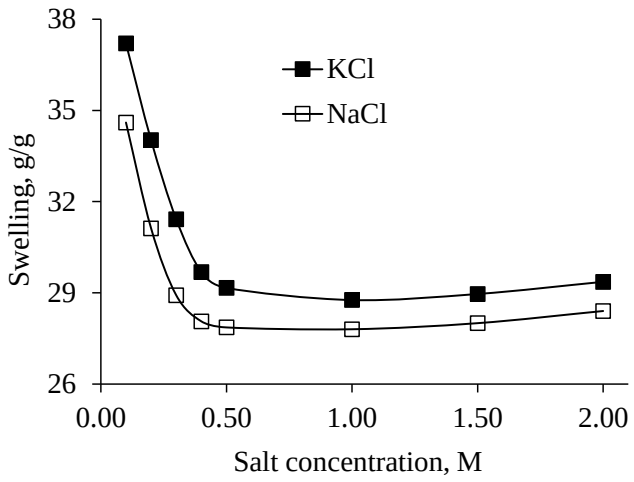


Fig. 2 Swelling behaviour of MPH in different concentrations of NaCl and KCl.

3.5 Swelling-deswelling kinetics in response to external stimuli

3.5.1 Swelling-deswelling behaviour of MPH in water and ethanol. The hydrogel deswells in ethanol rapidly because ethanol has less affinity with hydrogel than water (Fig. 3). MPH forms less hydrogen bonding with ethanol because it has low polarity and dielectric constant (24.55) than water (80.40). This lesser dielectric constant decreases ionization of

ionizable groups and swelling capacity of the polymer. Hydrogel swells again in water quickly due to swift wash out of ethanol molecules and formation of extensive hydrogen bonding with water.

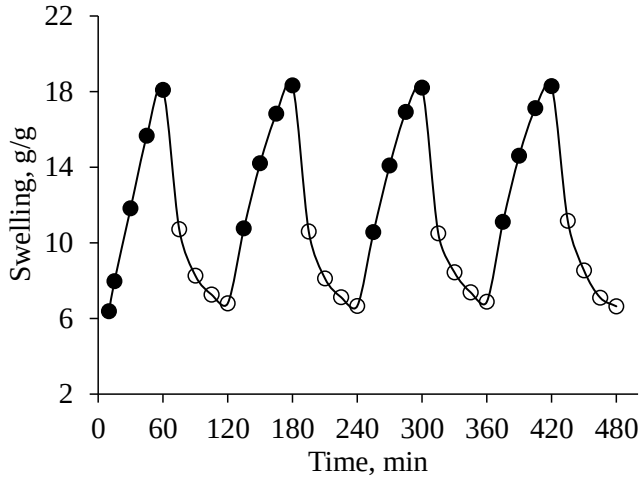


Fig. 3 Swelling-deswelling behaviour of MPH in deionized water (filled circles) and ethanol (empty circles).

3.5.2 Swelling-deswelling behaviour of MPH in acidic and basic buffers. Evaluation of swelling-deswelling behaviour of hydrogel was carried out using different buffers. MPH swells in basic buffer (pH 7.4) whereas deswells in acidic buffer (pH 1.2). This swelling-deswelling behaviour of MPH was noted four times and results of these on-off experiments are shown in Fig. 4. The mechanism of swelling-deswelling behaviour of MPH has already been discussed in section 3.2.

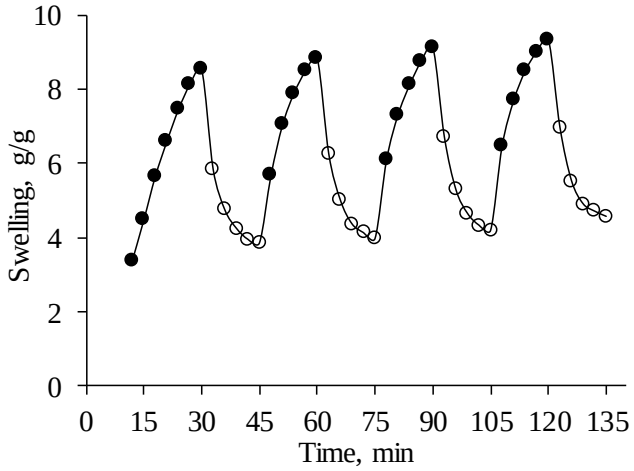


Fig. 4 Swelling-deswelling behavior of MPH in basic (filled circles) and acidic (empty circles) buffers.

3.5.3 Swelling-deswelling behaviour of MPH in deionized water and NaCl solution.

Swelling and deswelling of MPH was studied by immersing MPH in water and NaCl solution (0.9%) respectively. It was found that MPH shows swelling in water while shrinking in salt solution when studied at regular intervals (Fig. 5). Actually, addition of salt decreases the osmotic pressure between hydrogel and water. In this way, water molecules move out of hydrogel and swelling decreases.[38,39]

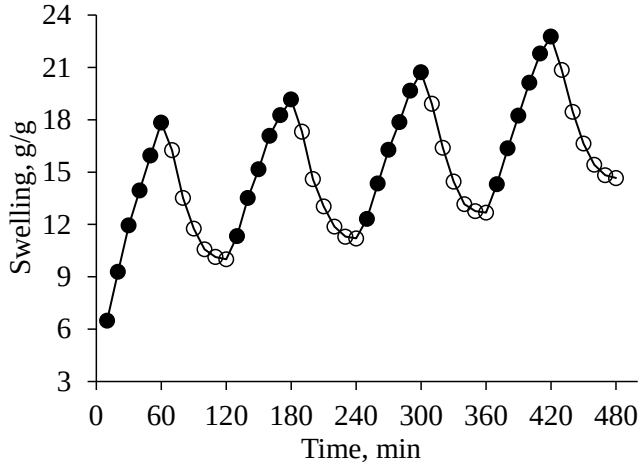


Fig. 5 Swelling-deswelling behaviour of MPH in deionized water (filled circles) and NaCl solution (empty circles).

3.6 Scanning electron microscopy (SEM)

The surface morphology and porosity of swollen then freeze-dried MPH were investigated with SEM. The SEM images of transverse cross sections of hydrogel (Fig. 6) confirm the presence of interconnected macropores in the size range of 5-147 μm. The average pore size (of macropores) measured with Image J software was 62.94 μm. The SEM analysis of longitudinal cross sections of hydrogel reveals that the interconnected macropores are arranged in the form of hollow macroporous channels, responsible for the fast transportation of water or other solvent. It is therefore expected that MPH may be used in drug release, cosmetics, diapers and pharmaceuticals.

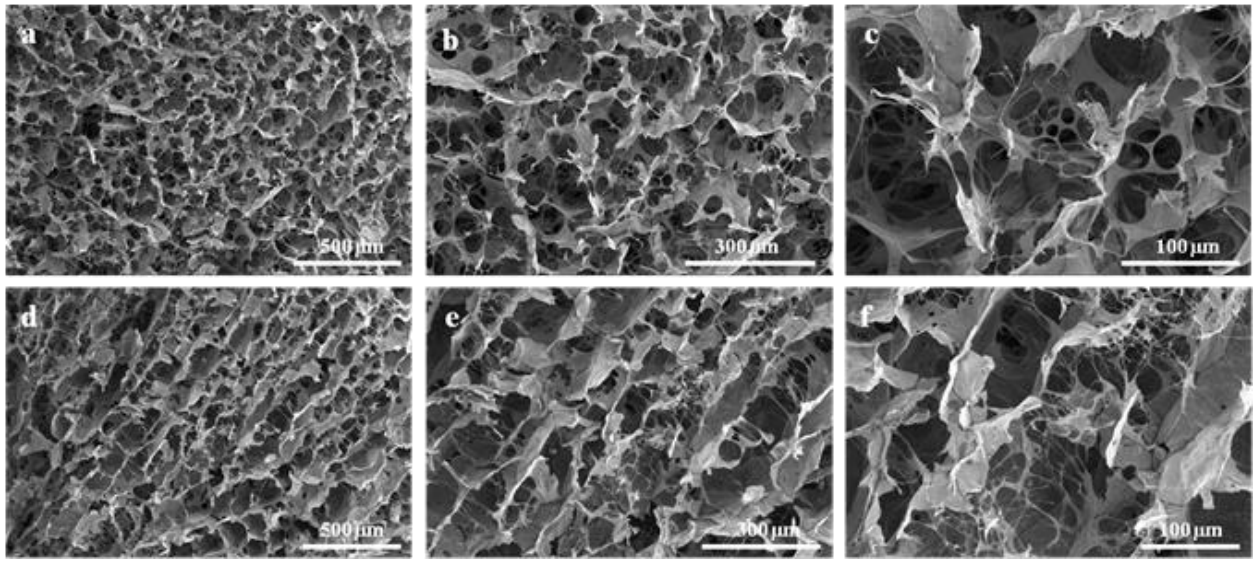


Fig. 6 Scanning electron micrographs of transverse (a, b and c) and longitudinal (d, e and f) cross sections of swollen then freeze-dried MPH (with average pore size 62.94 μm) at different magnifications. Size distribution of macropores (g) and (h); of transverse (a) and longitudinal (d) cross sections.

3.7 *In-vitro* drug release mechanism

Drug release from the water-swellable polymeric drug delivery systems is mainly controlled by swelling capability of hydrogel, solubility of drug in the dissolution media and interaction between hydrogel and drug.[40] Release behaviour of DS from MPH containing tablets was evaluated in SGF and SIF for 2 and 14 h, respectively. For this purpose, different formulations of DS by varying the amount of MPH were prepared (see Table 1). The release in SGF was found to be lesser due to low swelling capacity of hydrogel and insolubility of DS in acidic media. The release of DS in SGF was found to be 4.8, 4.5 and 3.75% for F1, F2 and F3, respectively. In SIF, swelling capacity of hydrogel and dissolution of DS increases due to slightly basic media, therefore, release of DS (after 14 h in SIF) was noted to be 97.21, 96.3 and 80.8% for F1, F2 and F3, respectively. It was also observed that with increase in concentration of MPH in DS formulations, release of drug decreases. Formulation F3 sustained the drug better than commercially available Voltral® SR tablet formulation. The results of drug release studies are shown in Fig. 7a.

The values of n and k_p were calculated from the slope and intercept of the plot of $\ln(M_t/M_\infty)$ vs $\ln t$, respectively and given in Table 3. The values of n range from 0.894-0.944 for the given

formulations, which indicates that the drug release follows the super case-II transport mechanism in which the release of drug is governed by erosion of the delivery system.

Swelling behaviour of all three formulations (F1, F2 and F3) were evaluated in water and results are depicted in Fig. 7b. It was observed that the swelling of tablets are directly proportional to the concentration of MPH in tablet formulations. Fig. 7c has shown the condition of tablet (F1) during swelling process in water after selected time intervals.

Morphology of the MPH (air-dried) and the tablet of DS containing MPH (F3) were observed by SEM analysis (see Fig. 7d). Results of SEM revealed that appearance of the MPH was like micro-flakes. On pressing into the tablet the surface become smooth but showing some nanopores and micro cracks which further support the superporous and superabsorbent nature of MPH that is a prerequisite for a polysaccharidal materials for sustained/controlled release of drugs.[41]

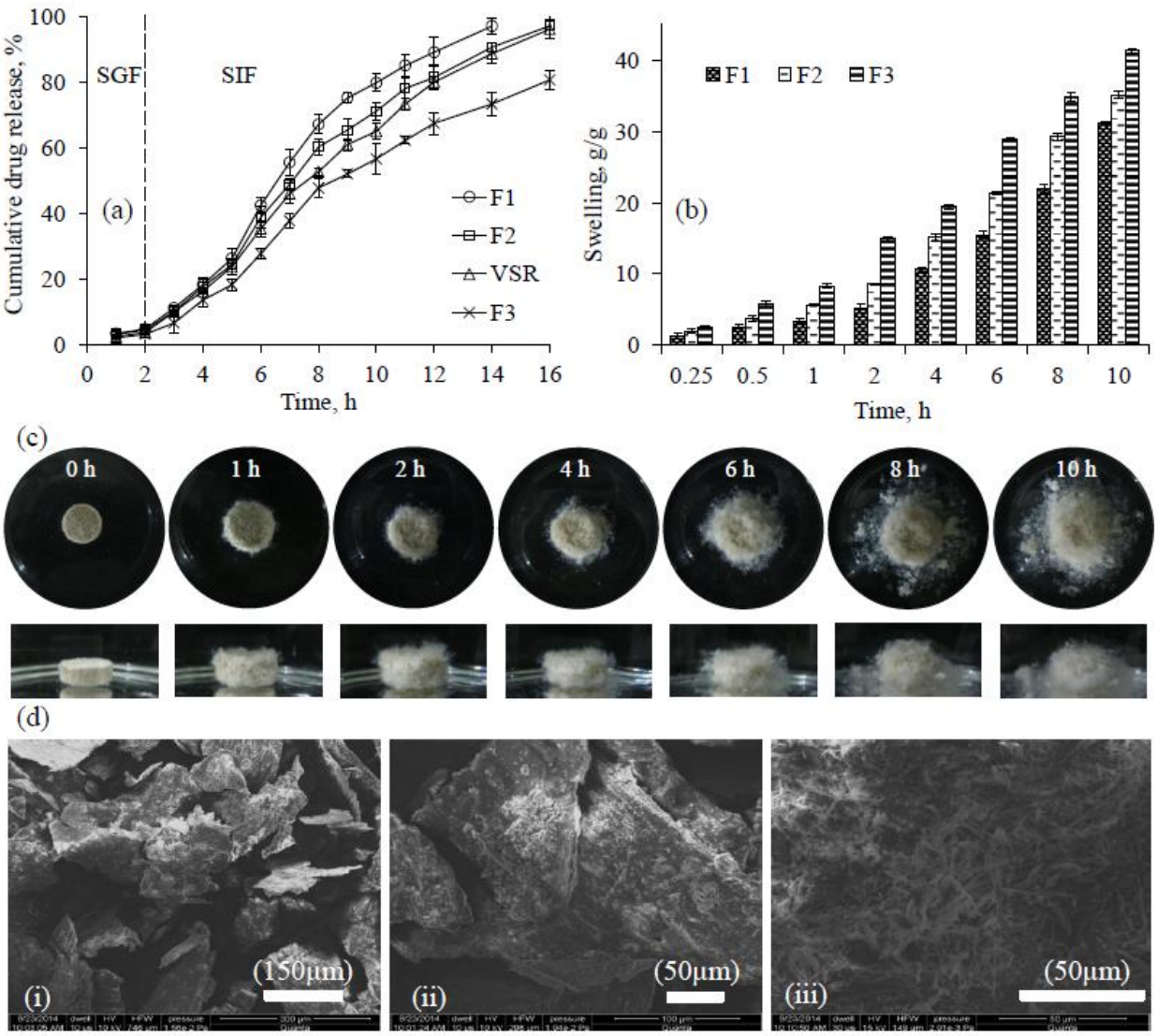


Fig. 7 (a) Drug (DS) release profile from MPH matrix tablets in SGF and SIF, (b) Swelling capacity of MPH tablets containing DS, (c) photographs exhibiting swelling behaviour (aerial and axial view) of F1 formulation in water and (d) SEM images of air-dried hydrogel (i and ii) and tablet (F1) surface (iii).

Table 3 Mathematical data of power law

Formulation	n	k_p	r^2
F1	0.899	12.554	0.9699
F2	0.894	11.603	0.9745
F3	0.944	9.966	0.9752

4 Conclusions

Mimosa pudica hydrogel has shown high swelling in deionized water, at pH 6.8 and 7.4 while unable to show reasonable swelling at pH 1.2. Furthermore, excellent stimuli responsive swelling-shrinking behaviour of *Mimosa pudica* hydrogel in water and ethanol, in basic (pH 7.4) and acidic (pH 1.2) media and in water and normal saline solution has proved its potential as an intelligent drug delivery system. SEM analysis has confirmed the macroporous nature of freeze dried hydrogel which made it a superabsorbent material for many pharmaceutical applications. *In vitro* drug release study has shown that *Mimosa pudica* hydrogel is a potential candidate for sustained and targeted delivery of drugs in small intestine and colon.

Acknowledgements

G. Muhammad gratefully acknowledges the Higher Education Commission, Pakistan, for funding under the scheme "HEC Indigenous 5000 Fellowships".

References

1 E. N. Bum, D. L. Dawack, M. Schmutz, A. Rakotonirina, S. V. Rakotonirina, C. Portet, A. Jeker, H. R. Olpe and P. Herrling, *Fitoterapia*, 2004, 75, 309–314.

2 B. Dinda, B. Ghosh, S. Arima, N. Sato and Y. Harigaya, *J. Indian Chem. Soc.*, 2006, 83, 1044–1046.

3 Y. Ke, J. An, L. Jie-Li and Z. Jian-Xin, *Chin. J. Anal. Chem*., 2007, 35, 739–742.

4 N. Balakrishnan, V. H. Bhaskar, B. Jayakar and B. Sangameswaran, *Phcog. Mag.*, 2006, 7, 973–976.

5 K. S. Girish, H. P. Mohanakumari, S. Nagaraju, B. S. Vishwanath and K. Kemparaju, *Fitoterapia*, 2004, 75, 378–380.

6 M. Molina, C. M. Contreas and P. Tellez-Alcantara, *Phytomedicine*, 1999, 6, 319–323.

7 S. K. Kumar and K. L. S. Kumar, *Der Pharm. Lett.*, 2010, 2, 261–264.

8 M. Khalid, J. K. Shah, D. K. Suresh, R. K. Singh, I. V. N. Reddy and S. Kumar, *Int. J. Green Pharm.*, 2011, 5, 75–78.

9 G. Muhammad, M. A. Hussain, I. Jantan and S. N. A. Bukhari, *Compreh. Rev. Food Sci. Food Safety*, 2015, DOI: 10.1111/1541-4337.12184.

10 R. Saraswat and R. Pokharkar, *Int. J. Pharm. Tech. Res*., 2012, 4, 93–98.

11 S. A. Hoffman, *Adv. Drug Deliver. Rev.*, 2002, 54, 3–12.

12 R. Po, *J. Macromol. Sci., Part C: Polym. Rev.*, 1994, 34, 607–662.

13 M. A. Hussain, G. Muhammad, I. Jantan and S. N. A. Bukhari, *Polym. Rev*., DOI: 10.1080/15583724.2015.1078351.

14 B. T. Good, C. N. Bowman and R. H. Davis, *Chem. Eng. Sci*., 2004, 59, 5967–5974.

15 D. Z. Liu, M. T. Sheu, C. H. Chen, Y. R. Yang and H. Ho, *J. Control. Release*, 2007, 118, 333–339.

16 Z. Zhao, *Chem. Eng. J*., 2008, 142, 263–270.

17 Z. Liu, W. Toh and T. Y. Ng, *Int. J. Appl. Mechanics*, 2015, 7, 1530001–1530035.

18 W. Toh, T. Y. Ng, Z. Liu and J. Hu, *Poly. Int*., 2014, 9, 1578–1583.

19 A. Abbas, M. A. Hussain, M. Amin, M. N. Tahir, I. Jantan, A. Hameed and S. N. A. Bukhari, *RSC Adv.*, 2015, 5, 43440–43448.

20 M. T. Haseeb, M. A. Hussain, S. H. Yuk, S. Bashir and M. Nauman, *Carbohyd. Polym.*, 2015, 136, 750–756.

21 X. Zou, X. Zhao and L. Ye, *RSC Adv.*, 2015, 5, 96230–96241.

22 A. P. Gerola, D. C. Silva, S. Jesus, R. A. Carvalho, A. F. Rubira, E. C. Muniz, O. Borges and A. J. M. Valente, *RSC Adv.*, 2015, 5, 94519–94533.

23 C. Gao, J. Ren, W. Kong, R. Sun and Q. Chen, *RSC Adv.*, 2015, 5, 90671–90681.

24 Y. Qiu and K. Park, *Adv. Drug Del. Rev*., 2001, 53, 321–339.

25 Q. Tang, J. Wu and J. Lin, *Carbohyd. Polym*., 2008, 73, 315–321.

26 J. I. Well and M. E. Aulton, Preformulation. In M. E. Aulton (Ed.), Pharmaceutics; The science of dosage form design. Edinburgh: Churchill Livingstone, 1988, 223–253.

27 S. G. Ring, *Starch-Starke*, 1985, 37, 80–83.

28 J. Peerapattana, P. Phuvarit, V. Srijesdaruk, D. Preechagoon and A. Tattawasart, *Carbohydr. Polym*., 2010, 80, 453–459.

29 E. Diez-Pena, I. Quijada-Garrido and J. M. Barrales-Rienda, *Polymer*, 2002, 43, 4341–4348.

30 M. K. Krusic and J. Filipovic, *Polymer*, 2006, 47, 148–155.

31 R. W. Korsmeyer, R. Gurny, E. M. Doelker, P. L. Buri and N. A. Peppas, *Int. J. Pharm.*, 1983, 15, 25–35.

32 P. I. Ritger and N. A. Peppas, *J. Control. Release*, 1987, 5, 37–42.

33 J. Siepmann and N. A. Peppas, *Adv. Drug Deliv. Rev.*, 2001, 48, 139–157.

34 A. Pourjavadi, M. Sadeghi and H. Hosseinzadeh, *Polym. Adv. Technol*., 2004, 15, 645–653.

35 S. E. Park, Y. C. Nho, Y. M. Lim and H. I. Kim, *J. Appl. Polym. Sci.*, 2004, 91, 636–643.

36 Y. Zhao, W. Chen, Y. Yang, X. Yang and H. Xu, *Colloid Polym. Sci*., 2007, 285, 1395–1400.

37 M. K. A. Pourjavadi, *Eur. Polym. J*., 2007, 43, 877–889.

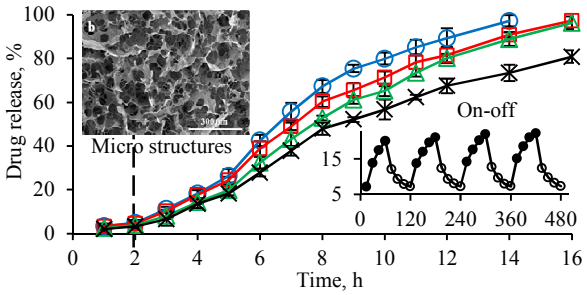
38 N. A. Peppas and A. G. Mikes, Hydrogels in Medicine and Pharmacy Vol.1, CRC Press: Boca Raton, FL, 1986.

39 G. Pass, G. O. Philips and D. J. Wedlock, *Macromolecules*, 1977, 10, 197–201.

40 C. S. Brazel and N. A. Peppas, *Polymer*, 1999, 40, 3383–3398.

41 Y. Huang, H. Yu and C. Xiao, *Carbohydr. Polym.*, 2007, 69, 774–783.

Graphical Abstract



Polysaccharide based stimuli responsive, superporous and superabsorbent hydrogel for sustained drug release