

## Comparative Drug Loading and Release Study on Some Carbohydrate Polymers

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**SUMMARY.** Carbohydrate polymers isolated from seeds of *Salvia plebeia*, *Mimosa pudica*, *Lallemantia royleana*, *Ocimum basilicum* and *Plantago ovata*, *P. ovata* husk, and gums of *Acacia modesta* and *A. nilotica*, have been characterized and evaluated for their potential as drug release materials. Analysis showed that these are almost protein-free polysaccharides. Images obtained by time-of-flight secondary ion mass spectrometry of caffeine- and diclofenac sodium-loaded films of the polymers showed that these materials encapsulate the drugs with very high degree of uniformity. The pattern of drug uptake by the polymers differed significantly from each other. *O. basilicum* showed much higher uptake as compared with the others. The drug-loaded films exhibited sustained release *in vitro* over a period of about 30 h following a diffusion-swelling controlled mechanism. As compared with others *M. pudica* appears to provide a better release profile of the two different drugs (following the Higuchi model).

**RESUMEN.** Polímeros de carbohidratos aislados de semillas de *Salvia plebeia*, *Mimosa pudica*, *Lallemantia royleana*, *Ocimum basilicum* y *Plantago ovata*, cáscara de *P. ovata*, y gomas de *Acacia modesta* y *A. nilotica* se han caracterizado y evaluado por su potencial como materiales de liberación de fármacos. El análisis mostró que estos polisacáridos están casi libre de proteínas. Las imágenes obtenidas por el tiempo de vuelo de la espectrometría de masas de iones secundarios de las películas cargadas con cafeína y diclofenaco sódico de los polímeros mostraron que estos materiales encapsulan los fármacos con muy alto grado de uniformidad. El patrón de la captación del fármaco por los polímeros difería significativamente entre sí. *Ocimum basilicum* mostró mucho mayor captación en comparación con los otros. Las películas cargadas con fármaco mostraron una liberación sostenida *in vitro* durante un período de aproximadamente 30 h mediante un mecanismo controlado de difusión-hinchazón. En comparación con otros, *Mimosa pudica* parece proporcionar un perfil de liberación mejor de los dos fármacos (siguiendo el modelo de Higuchi).

### INTRODUCTION

Carbohydrate polymers are being studied to explore their potential in sustained release and targeted delivery of drug molecules<sup>1,2</sup>. They are attractive materials due to their abundant availability, biocompatibility, biodegradability and low price. Most of the drug release studies have been carried out on a selected polysaccharide material<sup>1,3</sup> or a composite thereof<sup>4</sup>. In order to evaluate these materials for the intended use, it is desirable to have a comparative knowledge of the properties of related polysaccharides under similar working conditions. We are engaged in a

comprehensive study of several mucilages of diverse materials isolated from *Salvia plebeia*, *Mimosa pudica*, *Lallemantia royleana*, *Ocimum basilicum*, *Plantago ovata*, *Acacia modesta*, and *Acacia nilotica*, resulting in very useful information, which is presented in this paper. All of these materials are from renewable sources and abundantly available in most parts of the world. They form mucilage in water. A detailed thermal analysis of these materials has already been reported by our group<sup>5</sup>. This analysis revealed that they are robust materials for their use in drug delivery and their degradation products are

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non-toxic and benign to the environment. These materials do not adversely affect the immune system <sup>1</sup>.

The objectives of the present work were to study: i) absorption of caffeine and diclofenac sodium, as model drugs, from their solutions by the carbohydrate polymers isolated from the plant materials as identified above, and ii) study drug distribution pattern in these polymers by use of time-of-flight secondary ion mass spectrometry (ToF-SIMS), a newly developed technique for mapping chemicals dispersed in polymers. ToF-SIMS is emerging as a powerful technique that can map distribution of a chemical compound dispersed in a polymer matrix with high spatial resolution. This technique has been used to study surface chemistry of materials at a spatial resolution around 1  $\mu\text{m}$  <sup>6,7</sup>. There are also some examples of application of ToF-SIMS to study drug distribution in drug delivery systems <sup>8</sup>. The technique involves rastering of a cluster ion beam onto the surface of the sample, which results in generation of secondary ions through a cascade of collisions. These ions are accelerated into time-of-flight tube and resolved therein. The advantages of this technique include high mass resolution ( $> 7,000$ ), a large mass range (element to a complex molecular mass), excellent spatial resolution and an ability to simultaneously detect fragment ions over a large mass range <sup>9</sup>. The technique allows several samples to be loaded on to the cryo-stage and analyzed consecutively.

## MATERIALS AND METHODS

### Materials

The materials and chemicals used in this study were: *S. plebeia* seeds, *M. pudica* seeds, *L. royleana* seeds, *O. basilicum* seeds, *P. ovata* seeds and husk, *A. modesta* gum, *A. nilotica* gum (all purchased from Kohenoor International (Pvt) Ltd, Hyderabad, Pakistan); L-(+)-arabinose, D-(+)-galactose, D-glucose, D-(+)-xylose, L-rhamnose monohydrate (all from Sigma-Aldrich, USA) as standards for monosaccharide analysis; BCA protein assay reagents A 23228, B 23224 and albumin standard 23209 (Thermo Scientific, Pierce, USA) for protein analysis; Pullulan and dextran (Sigma-Aldrich, USA) as standards for gel permeation chromatography; citric acid (E. Merck, Germany), disodium hydrogen phosphate (E. Merck, Germany) for buffer preparation; and hydrochloric acid (E. Merck, Germany)

for dissolution medium. All the chemicals were used without further purification. Distilled water was used throughout this study.

### Isolation of carbohydrate polymers

#### **Mucilage of *P. ovata*, *O. basilicum*, *M. pudica*, and *L. royleana* seeds and *P. ovata* husk**

The seeds were de-dusted by sifting, weighed (50 g) and soaked in distilled water (2.5 L) separately for about 24 h. The swollen material was blended by use of a kitchen blender (1L, Panasonic MX-151SP1WRA) for 2-3 min intermittently, taking care that the seeds do not break. The mucilage was separated by filtration through muslin cloth (maximum pore size 1 mm) under vacuum ( $1.5 \times 10^{-2}$  mbar; Edwards rotary pump E2M28). The volume of filtrate was reduced to approximately 100 mL by evaporation in a rotary evaporator (Rotavapor® R-210, BÜCHI Labortechnik AG, Switzerland) at about 30 °C. The semi-dry material was spread on polyethylene sheet and allowed to air-dry at room temperature (~25 °C) for one week to obtain a film having thickness 0.07-0.15 mm. The glass surface was not suitable for this purpose as the polymers stuck to it due to high adhesive power. The yields were approximately 12% (*M. pudica*, *L. royleana*, *O. basilicum*, and *P. ovata* seeds) and 25% (*P. ovata* husk) w/w. The yield was calculated from the weight of seeds after dedusting and the weight of the films excluding moisture content.

#### **Mucilage of *S. plebeia* seeds**

The mucilage was prepared as above by excluding the blending step because of the softness of these seeds. The film thickness was 0.24 mm and yield was approximately 10% w/w.

#### **Purification of *A. modesta* and *A. nilotica* gums**

The *A. modesta* and *A. nilotica* gums (20 g each) as obtained from the market were freed from extraneous matter by dissolving them in water (150 mL) separately. The solutions were filtered through muslin cloth (maximum pore size 1 mm) under vacuum. The volume of the filtrate was reduced to approximately 30 mL by evaporation in a rotary evaporator at about 30 °C. The thick paste was spread on polyethylene sheets and air-dried at room temperature (~25 °C) for five days to obtain a film having thickness 0.22-0.25 mm. The yields were approximately 98%. All the isolated plant materials were used to prepare drug-loaded films.

## Characterization

### Composition

Elemental analysis of the isolated materials was performed by use of CHNS analyzer Vario MICRO V1.4.2 (Elementar Analysensysteme, GmbH, Germany). Moisture content was determined by Karl-Fischer titration using 701KF Titrino (Metrohm, Switzerland). Monosaccharide analysis was performed after hydrolysis with sulfuric acid<sup>10</sup>, by using Dionex ICS 3000 HPLC system consisting of: CarboPacPA20 column (150 × 0.4 mm; 6.5 μm) and electro chemical detector according to a reported method<sup>11</sup>. Protein content of the polymers was determined by bicinchoninic acid (BCA) assay<sup>12</sup>.

Molar masses were determined by gel permeation chromatography (GPC) using Agilent 1200 series (Agilent, Germany) system equipped PL aquagel-OH mixed column and refractive index detector (G1362A) using water as eluent (flow rate 1.0 cm<sup>3</sup>/min at 70 °C) and injection volume of 10 μL. Pullulan and dextran were used as calibration standards.

FT-IR spectra of the polymer films (un-loaded and drug-loaded) were recorded on FT-IR 640 (Varian, USA). Differential scanning calorimeter (DSC) of the pure drugs, un-loaded and drug-loaded polymers were carried out on SDT, Q-600 (TA instruments, USA) thermal analyzer at 10 °C min<sup>-1</sup> heating rate under nitrogen atmosphere.

### Scanning electron microscopy (SEM)

SEM images were obtained by Hitachi S-3400N and Jeol JSM-6060 LV machine. The polymer films (blank and drug-loaded) were mounted on aluminum stubs with the help of silver paint and sputter coated with gold. The images were recorded, by applying 10 kV accelerating voltage, at different magnifications.

### Drug loading and ToF-SIMS analysis

Drug-loaded polymer films are among important drug-delivery devices. They are used to prepare controlled-release formulations for ophthalmic inserts and suspensions<sup>13</sup> and mucoadhesive systems<sup>14</sup>. Most commonly used polymers for these applications include hydroxypropylmethyl cellulose, poly lactic acid, polyglycolic acid, carbodiimide crosslinked hyaluronic acid (HA) films and 2-hydroxyethyl methacrylate<sup>13,14</sup>. These materials are synthetic or semisynthetic and very expensive. The materials under investigation on the other hand are highly biocompatible, obtainable from renewable sources and highly economical. Thus drug-

loaded films were prepared from the materials under investigation and evaluated. Small pieces (3 × 3 mm<sup>2</sup>) of the individual polymer films were immersed in 1% caffeine (20 mL) and 2% diclofenac sodium (20 mL) aqueous solutions separately for 15 min. The drug-loaded polymers were removed from the solutions, briefly rinsed in distilled water to remove the drug particles sticking to the surface of the polymer, air-dried on the polythene sheets at room temperature for 24 h and subjected to ToF-SIMS analysis. ToF-SIMS measurements were carried out by use of the Ion-TOF IV (ION-TOF GmbH, Germany) using a Bi<sup>3+</sup> cluster source and a single-stage reflectron analyzer. Spectra were acquired in positive and negative modes by rastering primary ion energy of 25 kV, along with a pulsed target current of approximately 1 pA and post-acceleration energy of 10 kV across the sample surface. The area analyzed was 225 × 225 μm at a resolution of 225 × 225 pixels. The primary ion dose density was maintained at < 1012 ions/cm<sup>2</sup> to ensure static conditions. Data were processed by use of imaging software (Surface Lab 6 Image; ION-TOF GmbH).

### Drug release study

The drug release was studied by use of drug-loaded films. The polymer (5 g) was soaked in 300 mL of the drug solution (1% w/v in water) for 2 h and centrifuged by use of glass tubes fitted with a permeable bottom (Roth Filter Tubes LE72.1, porosity 1). The wet material was spread on a polyethylene sheet by use of a spreader and air-dried for one week to obtain the drug-loaded film of uniform thickness (0.2 mm). The film was cut into pieces (3 × 3 cm<sup>2</sup>), which contained about 10 mg of the drug. The polymer film containing 10 mg of the drug was transferred to a dialysis tube. The tube was attached to the paddle of the USP dissolution apparatus type II and immersed in the dissolution medium (900 mL). The dissolution was studied in distilled water (for caffeine as its solubility is pH independent), 0.1M HCl (for diclofenac sodium as it is insoluble at a basic pH) and pH 6.8 phosphate buffer (for diclofenac sodium as directed by US Pharmacopeia). The USP apparatus was operated at 37 ± 0.1 °C and 50 rpm for diclofenac sodium and at 100 rpm for caffeine as directed by US Pharmacopeia. Samples (2 mL) were withdrawn at 15 min, 30 min, 45 min, 60 min, 120 min, and 180 min intervals up to 30 h, filtered, suitably diluted and assayed spectrophotometrically at 273 nm ( $\epsilon = 9124.045$ ;  $y =$

0.056x - 0.1705 with  $R^2 = 0.9998$ ) for caffeine, 275 nm ( $\epsilon = 10181.45$ ;  $y = 0.0366x - 0.0501$  with  $R^2 = 0.9994$ ) for diclofenac sodium in the buffer solution and 276 nm ( $\epsilon = 380.084$ ;  $y = 0.1024x + 0.0095$  with  $R^2 = 0.9864$ ) for diclofenac sodium in 0.1N HCl. The  $\epsilon$  values were determined experimentally. The measurements were made on UV-Vis spectrophotometer (Shimadzu, Japan). After each withdrawal an equal volume of the dissolution medium was replaced immediately. The study was performed in triplicate. The cumulative release (percent of the drug amount in the film) was plotted against time. The data were fitted into zero order<sup>15</sup>, first order<sup>16</sup>, Higuchi<sup>17,18</sup>, Hixson-Crowell cube root law<sup>19</sup> and Korsmeyer-Pappas<sup>20-24</sup> models in order to determine the release pattern and mechanism.

## RESULTS AND DISCUSSION

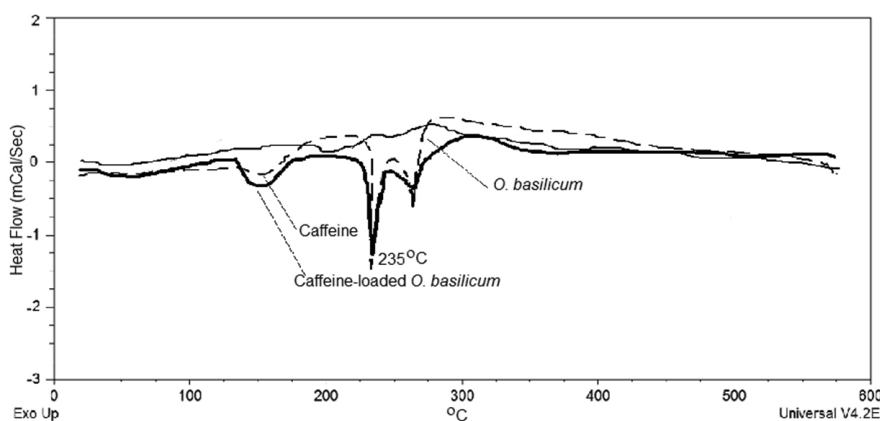
### Isolation and characterization

The isolated materials were white to light brown in color and characterized to be carbohydrate polymers by elemental, monosaccharide and protein analysis. Average percentages of

carbon and hydrogen in the isolated polymers were found to be 28.75 and 4.33% respectively (Table 1). The average C/H ratio in the polymers under investigation was 6.64, which is slightly lower than those reported for similar materials. Average percentage of sulfur and nitrogen is 0.14 and 0.61 which is less than 1% and can be considered as negligible. The analytical data was comparable with those of previously reported for such materials<sup>1,25</sup>. The protein content was < 0.5% (Table 1), therefore, these polymers can be considered as pure polysaccharides. Moisture content as determined by Karl-Fischer method ranged from 0.40% to 14.81% (Table 1); it was used for calculations on dry substance basis and explaining the mechanical properties. The uronic acid content could not be determined. The results of monosaccharide analysis after hydrolysis with  $H_2SO_4$  are given in Table 1. The monosaccharide contents of *A. nilotica* and *P. ovata* seeds and husk found in the present work are comparable with the literature values<sup>25-30</sup>. The monosaccharide content of *M. pudica* has previously been reported in a

Plant material	Monosaccharide content (% of total monosaccharides)					Elemental analysis (%)			Protein (%)	Moisture (%)
	Arabinose	Galactose	Glucose	Xylose	Rhamnose	C	H	N		
<i>S. plebeia</i> (S)	-	-	-	100	-	20.95	3.11	0.96	0.41	7.15
<i>S. plebeia</i> (M)	-	-	-	99.32	0.68					
<i>A. nilotica</i> (S)	74.17	25.83	-	-	-	33.82	5.191	0.35	0.09	4.77
<i>A. nilotica</i> (M)	75.74	24.26	-	-	-					
<i>M. pudica</i> (S)	-	-	30.89	69.11	-	29.72	4.62	0.78	0.26	0.40
<i>M. pudica</i> (M)	-	-	-	100	-					
<i>P. ovata</i> husk (S)	23.11	-	-	76.89	-	31.59	4.66	1.20		8.24
<i>P. ovata</i> husk (M)	21.37	-	-	78.63	-					
<i>A. modesta</i> (S)	68.09	30.11	-	-	1.79	34.27	5.25	0.21	0.13	5.23
<i>A. modesta</i> (M)	67.88	29.99	-	-	2.13					
<i>L. royleana</i> (S)	16.39	7.55	63.90	1.19	10.97	36.96	5.36	1.77		11.96
<i>L. royleana</i> (M)	29.14	1.28	-	-	69.59					
<i>O. basilicum</i> (S)	9.82	5.59	55.84	19.10	9.66	27.18	4.20	0.56		14.81
<i>O. basilicum</i> (M)	20.39	11.67	21.35	23.31	23.27					
<i>P. ovata</i> seeds (S)	21.90	-	-	78.10	-	30.37	4.43	0.43	0.34	10.2
<i>P. ovata</i> seeds (M)	18.99	-	-	81.01	-					

**Table 1.** Monosaccharide, elemental, protein and moisture analyses of polysaccharides obtained from different plant materials. S: after hydrolysis under severe conditions and M: hydrolysis under mild conditions as described in ref<sup>10</sup>.



**Figure 1.** DSC scans of blank and caffeine-loaded film of *O. basilicum* showing the melting peaks of the drug at 235 °C in both.

study carried out in 1956<sup>31</sup>, which showed the presence of xylose and glucuronic acid. Our results show the presence of xylose as the major and glucose as the minor components. Whereas, the contents of *S. plebeia*, *L. royleana* seeds and *A. modesta* have been determined for the first time. In case of *O. basilicum* varying results have been reported<sup>32-36</sup>; our results are closer to those reported in reference<sup>36</sup>. The only study available for *S. plebeia* is that reporting isolation of mucilage from the whole plant<sup>37</sup>. Based on these analyses the polymers can be classified as: rhamnoxylan (*S. plebeia*), galactoarabinan (*A. nilotica*), glucoxylan (*M. pudica*), arabinoxylan (*P. ovata*), galactoarabinan with little bit of rhamnose (*A. modesta*), xylogalactorhamnoarabinoglucan (*L. royleana*), galactorhamnoarabinoxylloglucan (*O. basilicum*). The weighted-average molar masses as determined by GPC were  $2.47 \times 10^6$  (*S. plebeia*),  $5.05 \times 10^5$  (*A. nilotica*),  $2.3 \times 10^6$  (*M. pudica*),  $3.26 \times 10^6$  (*P. ovata*),  $1.26 \times 10^6$  (*A. modesta*),  $3.5 \times 10^6$  (*L. royleana*) and  $4.9 \times 10^6$  (*O. basilicum*).

In the FT-IR spectra of un-loaded polymers characteristic bands due to  $\nu(\text{OH})$  at 3359-3463  $\text{cm}^{-1}$ ,  $\nu(\text{C}-\text{C})$  in arabinosyl side chain at 1000-1059  $\text{cm}^{-1}$ ,  $\beta$ -glycosidic C-H bending at 849-910  $\text{cm}^{-1}$ , and the out-of-phase bending of hydrogen bonded hydroxyl groups in the polymer backbone at 600-668  $\text{cm}^{-1}$  were observed. The absence of characteristic bands of proteins and ferulic acid indicated that the polymers under investigation were free from these materials. In the spectra of drug-loaded polymers additional bands due to drug molecules were observed. No new bands indicating any drug-polymer interaction were observed, which indicated the absence of such interactions. Similarly, no drug-polymer chemical interaction were indicated by the DSC data as the endothermic melting peaks

due to the drug molecules clearly observed in the DSC scans of drug-loaded polymers with the other features due to the polymers themselves remaining unchanged (Fig. 1).

#### SEM analysis

SEM images of the carbohydrate polymers were used to study their morphology and surface topography. As can be seen (Fig. 2) these polymers have different surface morphologies and consist of randomly distributed voids, which can be occupied by drug particles. The images of drug-loaded polymers are shown in Fig. 3, in which the dispersed drug particles can be visualized.

#### ToF-SIMS analysis

ToF-SIMS is a powerful technique for surface analysis and depth profiling of drug-loaded polymer films<sup>38</sup>. The spectra of the drugs, polymers (blank) and drug-loaded polymers are shown in Fig. 4. The  $m/z$  peaks at 22.9932, 39.0225 and 195.09 due to  $\text{Na}^+$ ,  $\text{C}_3\text{H}_3^+$  and  $\text{C}_8\text{H}_{11}\text{O}_2\text{N}_4^+$ , respectively, were considered as signatures of caffeine. Similarly, the peaks at 22.9932, 39.0225, and 339.92 due to  $\text{Na}^+$ ,  $\text{C}_3\text{H}_3^+$ , and  $\text{C}_{14}\text{H}_9\text{Cl}_2\text{NO}_2\text{Na}_2^+$ , respectively, were considered as signatures of diclofenac sodium. The results showed a uniform dispersion of caffeine particles in the polymer matrix of *S. plebeia*, *A. nilotica*, *A. modesta*, *M. pudica*, and *P. ovata* seeds and husk, while the dispersion was relatively less uniform in *L. royleana* and *O. basilicum*. In *S. plebeia* and *A. modesta* diclofenac sodium dispersed more uniformly than others. On the other hand the pattern of drug uptake was different in all the polymers (Fig. 4). This may be due to different solubility and hydrophilicity of the drug molecules, and structure of the polymers. In the present list the best up-

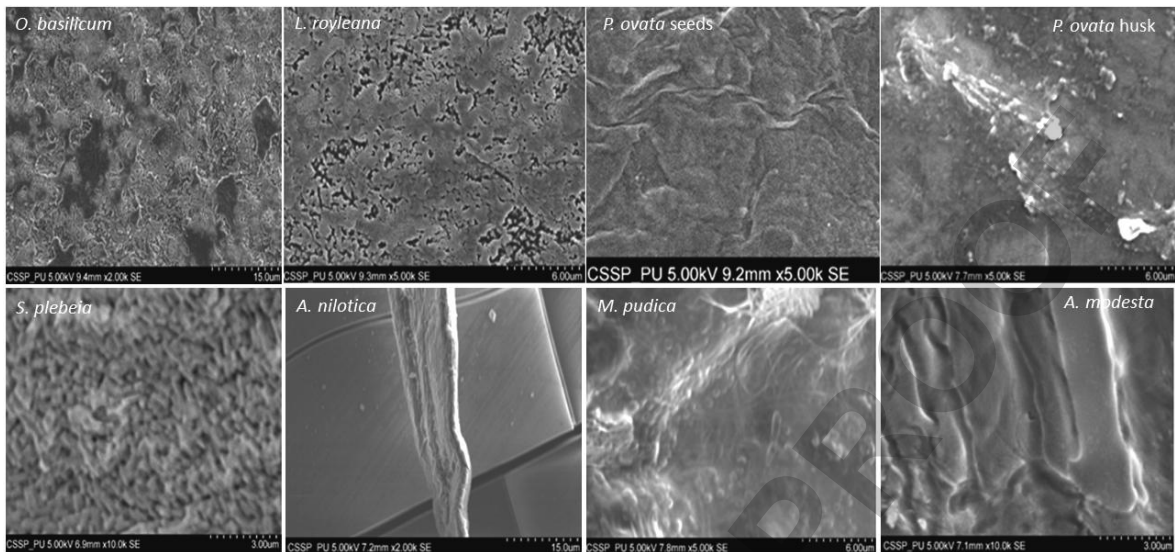


Figure 2. SEM images of blank polymer films.

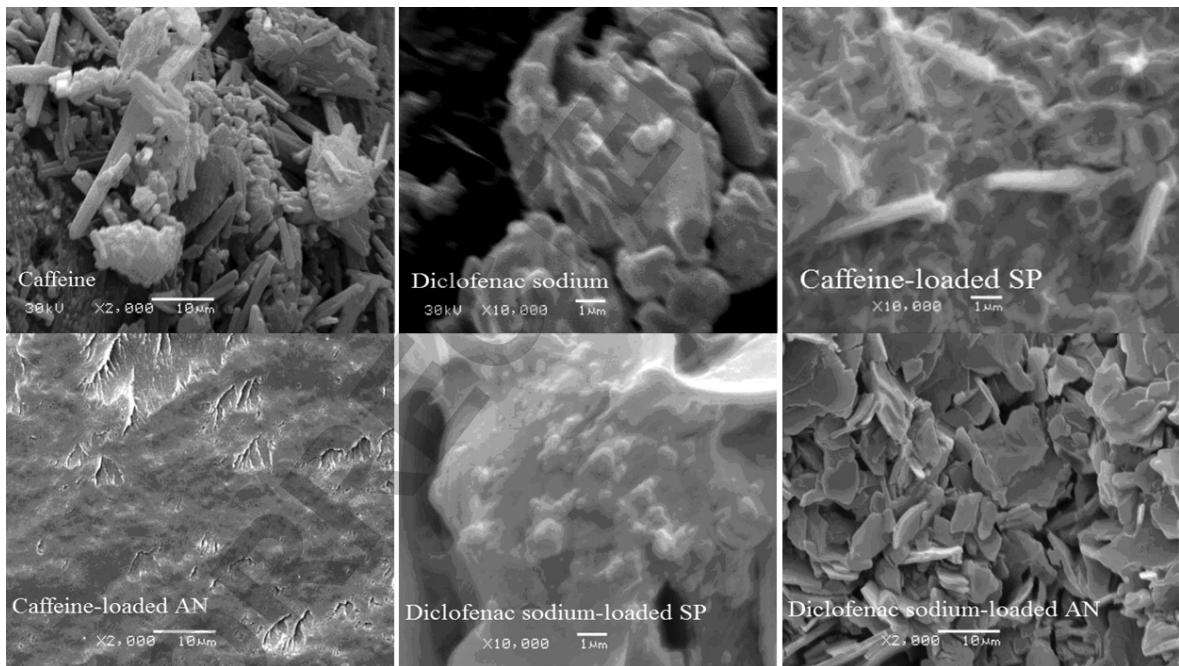


Figure 3 SEM images of pure drugs (caffeine and diclofenac sodium) and drug-loaded *S. plebeia* and *A. nilotica* films. The crystalline drug particles are clearly visible in the drug-loaded films.

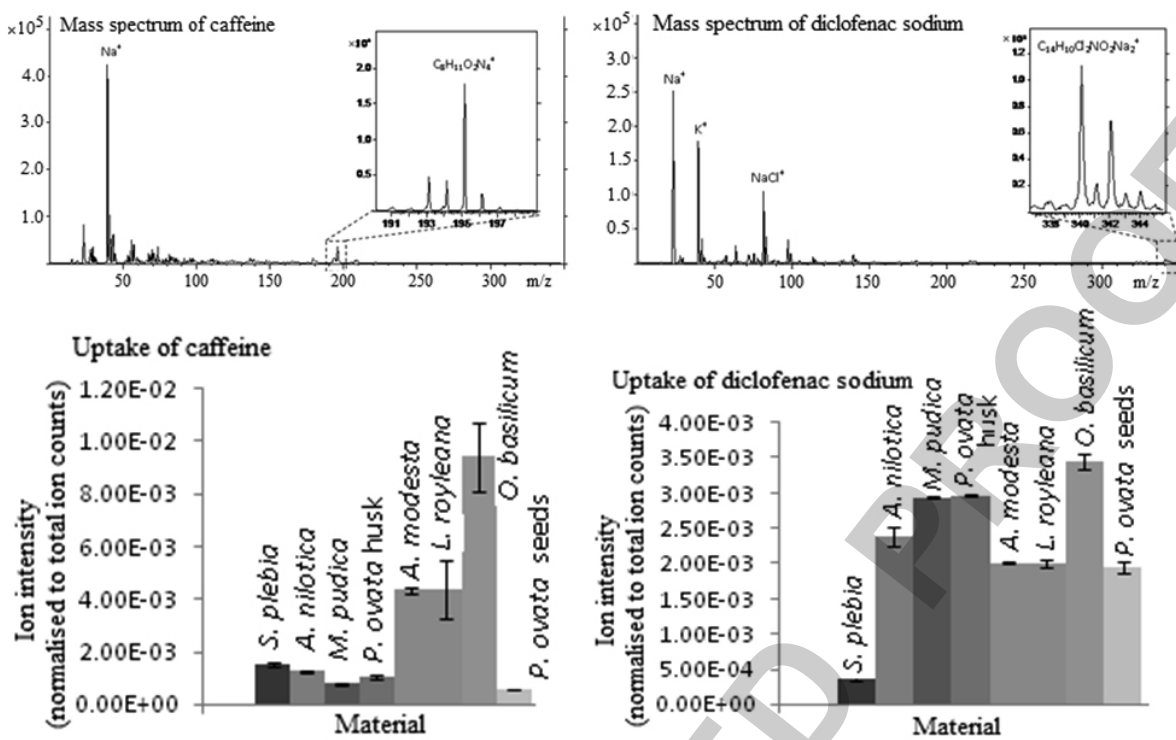
take was shown by *O. basilicum* for both the drugs.

### Drug release study

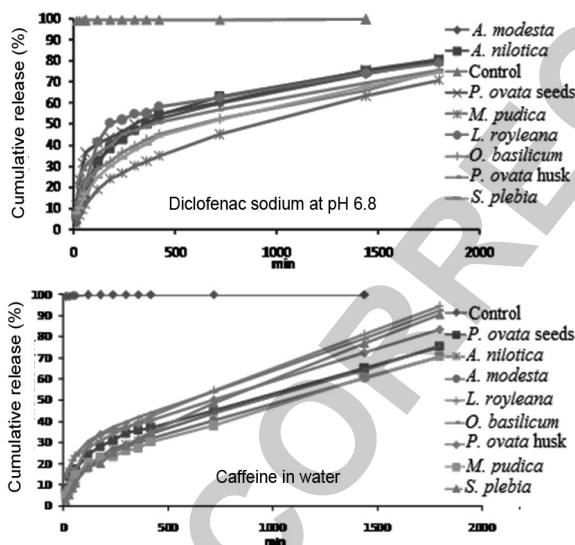
These materials under investigation absorb water on contact with biological fluids, swell and release the incorporated drug through diffusion, swelling, erosion or a combination thereof. To study the release kinetics and mechanism different models were applied in this work. The

release profiles of drug-loaded polymer films are shown in Fig. 5.

As compared with the solubility curve of naked drugs the polymers produced sustained release up to about 30 h. The release data were fitted into the five models. Of these Power Law, employing an empirical relationship, is considered more appropriate for determination of release mechanism of drugs from swellable polymeric systems to describe the Fickian, non-Fick-



**Figure 4** ToF-SIM analysis of drug loaded films showing mass spectra of the drug molecules (top), drug uptake by the polymers (bottom).



**Figure 5** Cumulative release of drugs from films in phosphate buffer pH 6.8 (diclofenac sodium) and distilled water (caffeine). The “control” curves represent dissolution of drugs excluding the polymers in the formulations.

ian and case-II transport mechanisms<sup>20,39</sup>. The release data of all the polymers for caffeine fitted well in Higuchi model followed by Power law (Table 2). In case of diclofenac sodium Higuchi (*M. pudica*, *O. basilicum* and *P. ovata*

husk), Power law (*A. modesta*, *A. nilotica* and *S. plebeia*), first order (*L. royleana*) and zero order (*P. ovata* seeds) were observed to be followed.

As far as release mechanisms as determined by Power Law are concerned, they were found to be: non-Fickian, *i.e.*, diffusion and swelling controlled (*A. modesta*, *A. nilotica*, *M. pudica*, *P. ovata* husk, and *S. plebeia* for caffeine and *A. modesta*, *A. nilotica*, *M. pudica*, *L. royleana*, *O. basilicum*, and *S. plebeia* for diclofenac sodium) and complex mechanism involving diffusion, swelling and erosion (*L. royleana*, *O. basilicum* for caffeine and *P. ovata* seeds and husk for diclofenac sodium). Whereas *P. ovata* seeds exhibited nearly Fickian, *i.e.*, only diffusion controlled mechanism for caffeine. The suggested mechanism was based on the *n* value according to the criteria: 0.45 (Fickian), 0.45 < *n* < 0.89 (non-Fickian) and *n* > 0.89 (super case-II). Thus these polymers appear to be suitable for formulation of various types of oral and ophthalmic solutions or suspensions.

The FT-IR and DSC analyses indicated that the drugs used in this study are not chemically bound with the polymers, therefore, it can be postulated that the drug solution is absorbed by the polymers when they are hydrated in the drug solution and drug particles are retained in

Material	Caffeine in distilled water						Diclofenac sodium in phosphate buffer (pH 6.8)							
	Zero order	First order	Higuchi	Hixson-Crowell	Power law	n	t <sub>50</sub> (min)	Zero order	First order	Higuchi	Hixson-Crowell	Power law	n	t <sub>50</sub> (min)
<i>A. modesta</i>	R <sup>2</sup>	0.950	0.989	0.996	0.950	0.997	0.496	0.733	0.909	0.908	0.733	0.905	0.621	360
	MSC	2.695	4.229	6.136	2.694	6.111		1.014	2.093	2.083	1.014	2.329		
<i>A. milotica</i>	R <sup>2</sup>	0.945	0.988	0.997	0.945	0.995	0.550	0.761	0.918	0.930	0.761	0.954	0.484	360
	MSC	2.599	4.18	5.677	2.599	5.188		1.125	2.204	0.396	1.125	2.790		
<i>P. ovata</i> seeds	R <sup>2</sup>	0.931	0.983	0.993	0.931	0.991	0.425	0.783	0.858	0.882	0.783	0.860	0.381	300
	MSC	1.362	3.780	4.658	2.374	4.418		3.444	1.553	1.739	1.128	1.567		
<i>M. pudica</i>	R <sup>2</sup>	0.954	0.986	0.985	0.954	0.974	0.530	0.899	0.976	0.993	0.899	0.955	0.630	920
	MSC	2.771	3.972	3.894	2.771	3.343		1.985	3.429	4.666	1.985	2.809		
<i>L. royleana</i>	R <sup>2</sup>	0.982	0.942	0.984	0.982	0.964	0.363	0.623	0.818	0.824	0.623	0.884	0.494	180
	MSC	3.712	3.558	3.836	3.712	3.030		0.668	2.563	1.432	0.669	1.849		
<i>O. basilicum</i>	R <sup>2</sup>	0.958	0.957	0.991	0.958	0.988	0.372	0.92	0.953	0.980	0.92	0.959	0.451	420
	MSC	3.347	2.853	4.435	2.869	4.186		2.126	2.674	3.547	2.126	2.798		
<i>P. ovata</i> husk	R <sup>2</sup>	0.903	0.975	0.982	0.903	0.979	0.482	0.852	0.949	0.973	0.852	0.995	0.259	420
	MSC	2.032	3.406	4.790	2.032	3.560		1.605	2.682	5.017	1.605	4.989		
<i>S. plebeia</i>	R <sup>2</sup>	0.970	0.970	0.992	0.970	0.983	0.694	0.860	0.961	0.980	0.860	0.987	0.472	720
	MSC	3.221	3.222	4.599	3.221	3.819		1.659	2.943	3.640	1.389	4.105		

**Table 2.** Fitness of release data of caffeine and diclofenac sodium from different film materials to various mathematical models.



the voids when they are dried. These materials are known to have good swelling properties <sup>1</sup>. The different behavior of the polymers under investigation can be attributed to different structure, size and shape of the voids, and swelling behavior.

## CONCLUSIONS

Protein-free polysaccharides isolated from various plant materials under investigation were evaluated for their potential as drug release materials. The polymers absorbed caffeine and diclofenac sodium (taken as model drugs) from their solutions to varying extent. The drug uptake and distribution was studied by ToF-SIMS, a powerful technique for profiling and imaging chemical substances in polymeric matrices. The results showed that the uptake trend was *O. basilicum* > *L. royleana* = *A. modesta* > *S. plebeiana* > *A. nilotica* > *P. ovata* husk > *M. pudica* > *P. ovata* seeds for caffeine and *O. basilicum* > *M. pudica* = *P. ovata* husk > *A. nilotica* > *A. modesta* = *L. royleana* = *P. ovata* seeds > *S. plebeia* for diclofenac sodium. Caffeine was found to be highly dispersed in *S. plebeia*, *A. nilotica*,

*A. modesta*, and *P. ovata* seeds and husk, whereas, diclofenac sodium was highly dispersed in *S. plebeia* and *A. modesta*. The drugs were moderately dispersed in other polymers. These variations are due to varying size of voids in the polymers as depicted by SEM images. The drug-loaded films exhibited sustained release *in vitro* over a period of about 30 h following a diffusion-swelling controlled mechanism. As compared with others *M. pudica* demonstrated a better release profile of the two model drugs.

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## REFERENCES

- Iqbal, M.S. J. Akbar, M.A. Hussain, S. Saghir & M. Sher (2011) *Carbohydr. Polym.* **83**: 1218-25.
- Akbar, J., M.S. Iqbal, M.T. Chaudhary, T. Yasin & S. Massey (2012) *Carbohydr. Polym.* **88**: 1348-57.
- Singh, K., A. Kumar, N. Langyan & M. Ahuja (2009) *AAPS Pharm Sci Tech.* **10**: 1121-7.
- Singh, B., G.S. Chauhan, S. Kumar & N. Chauhan (2007) *Carbohydr. Polym.* **67**: 190-200.
- Iqbal, M.S., S. Massey, J. Akbar, C.M. Ashraf & R. Masih (2013) *Food Chem.* **140**: 178-82.
- Scurr, D.J., T. Horlacher, M.A. Oberli, D.B. Werz, L. Kroeck, S. Bufali, *et al.* (2010) *Langmuir* **26**: 17143-55.
- Judd, A.M., D.J. Scurr, J.R. Heylings, K.W. Wan & G.P. Moss (2013) *Pharmaceut. Res.* **30**: 1896-905.
- Belu, A.M., M.C. Davies, J.M. Newton & N. Patel (2000) *Anal. Chem.* **72**: 5625-38.
- Chabala, J.M., K.K. Soni, J. Li, K L. Gavrilov & R. Levisetti (1995) *J. Mass Spec. Ion Processes* **143**: 191-212.
- Seaman, J.F., W.E. Moore, R.L. Mitchell & R.A. Millet (1954) *Tappi* **37**: 336-43.
- Weitzhandler, M., V. Barreto, C. Pohl, P. Jandik, J. Cheng & N. Avdalovic (2004) *J. Biochem. Biophys. Meth.* **60**: 309-17.
- Smith, P.K., R.I. Krohn, G.T. Hermanson, A.K. Mallia, F.H. Gartner, M.D. Provenzano, *et al.* (1985) *Anal. Biochem.* **150**: 76-85.
- Gaudana, R., J. Jwala, S.H.S. Boddu & A.K. Mitra (2009) *Pharmaceut. Res.* **26**: 1197-216.
- Jackson, J.K., K.C. Skinner, L. Burgess, T. Sun, W. L. Hunter & H.M. Burt (2002) *Pharmaceut. Res.* **19**: 411-7.
- Dash, S., P.N. Murphy, L. Nath & P. Chowdhury (2010) *Acta Pol. Pharm.-Drug Res.* **67**: 217-23.
- Gibaldi, M., S. Feldman (1967) *J. Pharmaceut. Sci.* **56**: 1238-42.
- Higuchi, T. (1961) *J. Pharmaceut. Sci.* **50**: 1145-9.
- Higuchi, T. (1963) *J. Pharmaceut. Sci.* **52**: 874-5.
- Hixson, A.W. & J.H. Crowell (1931) *Ind. Eng. Chem.* **23**: 923-31.
- Korsmeyer, R.W., R. Gurny, E. Doelker, P. Buri & N.A. Peppas (1983) *Int. J. Pharmaceut.* **15**: 25-35.
- Peppas, N.A. (1985) *Pharmaceut. Acta Helvet.* **60**: 110-1.

22. Ritger, P.L. & N.A. Peppas (1987) *J. Contr. Rel.* **5**: 23-36.
23. Ritger, P.L. & N.A. Peppas (1987) *J. Contr. Rel.* **5**: 37-42.
24. Grassi, M., R. Lapasn & S. Priel (1998) *Chem. Eng. Comm.* **169**: 79-109.
25. Saghir, S., M.S. Iqbal, M.A. Hussain, A. Koschella & T. Heinze (2008) *Carbohydr. Polym.* **74**: 309-17.
26. Elhadi, A.O.A. (2009) M.Sc. Thesis, Sudan University of Science and Technology.
27. Rassi, Z.E. (2002) *Elsevier B.V.*, pp. 891.
28. Laidlaw, R.A. & E.G.V. Purcival (1949) *J. Chem. Soc.* **1949**: 1600-7.
29. Fischer, M.H., N. Yu, G.R. Gray, J. Ralph, L. Anderson & J.A. Marlett (2004) *Carbohydr. Res.* **339**: 2009-17.
30. Laidlaw, R. A. & E.G.V. Purcival (1950) *J. Chem. Soc.* **1950**: 528-34.
31. Hulyakar, R. K., T. K. Ingle & B.V. Bhide (1956) *J. Indian Chem. Soc.* **33**: 864-5.
32. Anjaneyalu, Y.V. & R.N. Tharanathan (1972) *Curr. Sci.* **41**: 214.
33. Tharanathan, R.N. & Y.V. Anjaneyalu (1974) *Ind. J. Chem.* **12**: 1164-5.
34. Tharanathan, R.N. & Y.V. Anjaneyalu (1975) *Aust. J. Chem.* **28**: 1345-50.
35. Anjaneyalu, Y.V. & G.D. Channe (1979) *Carbohydr. Res.* **75**: 251-6.
36. Azoma, J. & M. Sakamoto (2003) *Trends Glycosci. Glycotechnol.* **15**: 1-14.
37. Huang, Y.L., C.F. Chau (2012) *Food Chem.* **133**: 1618-23.
38. Burns, S.A. & J.A. Gardella Jr. (2008) *Appl. Surf. Sci.* **255**: 1170-3.
39. Siepmann, J. & F. Siepmann (2008) *Int. J. Pharmaceut.* **364**: 328-43.

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