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Amylopectin-g-poly(N-vinyl-2-pyrrolidone): Synthesis, characterization and *in vitro* release behavior

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ABSTRACT

In the present study, amylopectin-g-poly(N-vinyl-2-pyrrolidone) was synthesized by UV-assisted grafting reactions. The effect of concentrations of amylopectin, N-vinyl-pyrrolidone and ammonium persulfate on the % grafting efficiency was studied using 3-factor, 2-level factorial experimental design. The graft co-polymer was characterized by Fourier-transform infrared spectroscopy (FT-IR), differential scanning calorimetry (DSC), X-ray diffraction (XRD) and scanning electron microscopy (SEM) studies. The concentrations of amylopectin, N-vinyl-2-pyrrolidone and ammonium persulfate were found to exert a significant synergistic effect on grafting efficiency. The optimized batch of graft co-polymer prepared using concentration of amylopectin (4%), N-vinyl-2-pyrrolidone (2%) and ammonium persulfate (10 mmol/L) had 83.16% grafting efficiency. On comparative evaluation of films of amylopectin-g-poly(N-vinyl-pyrrolidone) with amylopectin, the graft co-polymer film provided a prolonged release following Higuchi square release kinetics.

1. Introduction

Chemical modification of natural polymers can be achieved by variety of approaches such as etherification, cross-linking and graft co-polymerization (Rana et al., 2011). Grafting is a method where monomers are covalently bonded onto the polymer chain backbone. Grafting of polysaccharides with synthetic polymers can be used to design new materials with desirable release characteristics. Hybridization of natural polymer with synthetic polymers employing graft co-polymerization technique has been used as an approach to improve the functionality of natural polymers (Sen, Kumar, Ghosh, & Pal, 2009). There are reports based on earlier studies where properties of a wide range of natural polysaccharides like chitosan (Singh, Tiwari, Tripathi, & Sanghi, 2004), guar gum (Singh, Tiwari, Tripathi, & Sanghi, 2006), xanthan gum (Kumar, Singh, & Ahuja, 2009), tamarind and gum kongagogu (Malik & Ahuja, 2011) have been modified by grafting with a variety of vinyl monomers. Thus, in recent years, much attention has been paid on chemical modification of natural macromolecules (Sand, Mishra, & Behari, 2010). Various techniques of graft co-polymerization such as radiation, chemical initiation, *etc.*, have been reported in the literature (Bhattacharya & Misra, 2004).

Amylopectin (AMP), which constitutes 70–80% of starch is a highly branched polymer comprising of α-D-glucopyranosyl units containing 1,4-α-D-glucosidic linear linkages and 1,6-α-D-glucosidic linkages at the branched points (Fanta & Doane, 1986; Phillips, 1980). Amylopectin being a starch derivative is biocompatible, non-toxic, stable, biodegradable and low cost polymer. Till now, amylopectin has been explored as a polymer to prepare hydrophilic matrices, films or hydrogels for pharmaceutical applications (Nabais et al., 2007). During earlier studies graft co-polymers of amylopectin have been synthesized by grafting polyacrylamide (Singh, Nayak, Biswal, Tripathy, & Banik, 2003). In another study, amphoteric amylopectin has been synthesized by hydrolyzing amphoteric-g-poly(acrylamide) followed by cationization with N-(3-chloro-2-hydroxypropyl) trimethyl ammonium chloride (CHPTAC) (Singh, Pal, Rana, & Ghorai, 2013). In another study, graft copolymer of amylopectin and polyacrylic acid has been evaluated as high performance flocculants (Sarkar, Mandre, Panda, & Pal, 2013).

N-vinyl-2-pyrrolidone, a hydrophilic, non-toxic, biocompatible monomer (Lee, Park, & Robinson, 2000) has earlier been grafted on guar, carboxymethyl guar (Mishra, Yadav, Mishra, & Behari, 2011) and sodium alginate (Sand et al., 2010). Its copolymers and homopolymers have been used as an antimicrobial agent (Nud'ga et al., 2002), main component of temporary skin covers or wound dressing (Nho & Park, 2002) and also wrapping material (Ausman et al., 2001) of single-walled carbon nanotubes (SWNTs).

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In the present study, graft co-polymerization of N-vinyl-2-pyrrolidone on amylopectin was carried out employing UV-assisted grafting reactions. The preparation of graft co-polymer was optimized using 2-level, 3-factor full factorial experimental design. The optimized batch of amylopectin-g-poly(N-vinyl-2-pyrrolidone) was characterized by Fourier-transform infrared spectroscopy (FT-IR), differential scanning calorimetry (DSC), X-ray diffraction analysis (XRD) and scanning electron microscopy (SEM). Metronidazole, an anti-amoebic drug commonly used for treatment of periodontal diseases, which has earlier been tested in film formulations for local mucoadhesive delivery (El-Kamel, Ashri, & Alsarra, 2007), was employed as the model drug. Further, the graft co-polymer was evaluated for pharmaceutical applications by formulating films using metronidazole as the model drug. Films of amylopectin-g-poly(N-vinyl-2-pyrrolidone) were comparatively evaluated with the films of amylopectin for swelling and *in vitro* release studies.

2. Experimental

2.1. Materials

Amylopectin and N-vinyl pyrrolidone were purchased from Hi-Media Laboratories (Pvt.) Limited (Mumbai, India). Ammonium persulfate GR (purity 99%) was obtained from Loba Chemie Pvt. Ltd. (Mumbai, India). Glycerol was procured from Sisco Research Laboratory (Mumbai, India). Metronidazole was obtained as a gift sample from Ranbaxy Research Laboratories (Gurgaon, India). All other chemicals used were of reagent grade and used as such.

2.2. Preparation of graft co-polymer of N-vinyl-2-pyrrolidone and amylopectin

Graft co-polymerization of N-vinyl-2-pyrrolidone on amylopectin was carried out using UV-assisted graft co-polymerization reactions (Malik, Kumar, & Ahuja, 2012). Briefly, an aqueous solution of N-vinyl-2-pyrrolidone (1–2%, w/v) was added to amylopectin solution (3–4%, w/v) and dispersed by stirring, followed by addition of ammonium persulfate (0–10 mmol/L), a redox initiator. The solution so obtained was irradiated by short wave UV (*i.e.* UV-C) radiations in a UV chamber (TAB Machine; Mumbai, India) for 2 h to prepare various batches of grafted amylopectin (Table 1). The grafted copolymer was precipitated by pouring it into methanol to remove the unreacted monomer, separated by filtration, followed by drying in an oven at 40 °C to a constant weight. The grafting efficiency (% GE) was calculated using the following equation:

$$\text{Grafting efficiency } (\%) = \frac{W_1 - W_0}{W_2} \times 100 \quad (1)$$

where W_0 is the weight of amylopectin, W_1 the weight of the graft copolymer and W_2 the weight of NVP used.

2.3. Experimental design

2.3.1. Full factorial design

UV-assisted graft copolymerization of NVP on amylopectin was carried out using full factorial design. Factorial designs (FDs) are generally mathematical models. These are response surface experimental designs in which all levels of a given factor are combined with all levels of every other factor in the experiment. In the present study, graft copolymerization of N-vinyl-2-pyrrolidone on amylopectin, was optimized by two-level, three-factor, full factorial design. The concentrations of amylopectin, N-vinyl-2-pyrrolidone and ammonium persulfate were selected as the independent variables and percent grafting efficiency (%GE) was selected as the dependent variable (Table 1). Each independent variable was investigated at two levels, high level (+1) and low level (−1). All other variables were kept constant throughout the study. The design of experiment and statistical analysis of the data was done employing the Design Expert software (version 7.0.4.1, Stat-Ease Inc., Minneapolis, MN).

2.4. Characterization of amylopectin and amylopectin-g-poly(N-vinyl-2-pyrrolidone) graft copolymer

The graft co-polymer of N-vinyl-2-pyrrolidone and amylopectin was characterized by FT-IR spectroscopy, differential scanning calorimetry, X-ray diffraction, and scanning electron microscopy.

2.4.1. Fourier transform infra-red spectroscopy (FT-IR)

Grafting of N-vinyl-2-pyrrolidone on amylopectin was confirmed by subjecting the samples to FT-IR spectroscopy in Fourier-Transform infrared spectrophotometer (IR Affinity, Shimadzu, Japan). Samples were analyzed in the range of 4000–400 cm^{-1} as KBr pellets.

2.4.2. Differential scanning calorimetry (DSC)

Differential scanning calorimetric thermograms of amylopectin and grafted amylopectin were recorded in differential scanning calorimeter (Q10, TA Systems, USA). About 2 mg of dried samples were crimped and heated in standard aluminum pan over a temperature range of 40–350 °C at a rate of 10 °C/min with nitrogen purge of 50 ml/min.

2.4.3. X-ray diffraction analysis (XRD)

The powder X-ray diffraction pattern of amylopectin and grafted amylopectin was studied in X-ray diffractometer (Miniflex 2, Rigaku, Japan) with Nickel filtered Cu-K alpha radiation; at a voltage of 30 kV and current of 15 mA. Samples were scanned in the angular range of 0–70° diffraction angle (2θ) range with a scanning speed of 0.05 min^{-1}.

2.4.4. Scanning electron microscopy

The morphological features of amylopectin and grafted amylopectin were observed with SEM. The photomicrographs were recorded using scanning electron microscope (Hitachi, S-3400N, Japan). The specimens were mounted on the specimen stubs containing double adhesive carbon tape and coated with gold. These were recorded at an accelerating voltage of 10 kV at different magnifications.

2.5. Preparation of films of amylopectin and amylopectin-g-poly(N-vinyl-2-pyrrolidone)

Graft copolymer of amylopectin and NVP was explored for pharmaceutical applications by preparing films using metronidazole as the model drug. The films of amylopectin-g-poly(N-vinyl-2-pyrrolidone) and amylopectin containing metronidazole were prepared by solvent casting method. Briefly, an aqueous dispersion of amylopectin or amylopectin-g-poly(N-vinyl-2-pyrrolidone) (4%, w/v) was prepared by heating to 90 °C for 15 min (Rindlav-Westling, Stading, Hermansson, & Gatenholm, 1998). To this, metronidazole (0.05%, w/v) and glycerol (1%, w/v) as a plasticizer were added with the aid of stirring. The homogeneous dispersion was then poured on petriplates, cooled and dried in an oven at 40 °C for 24 h.

Table 1
Three factor, 2-level full factorial design for the synthesis of amylopectin-g-poly(N-vinyl-2-pyrrolidone).

Run	Conc. of amylopectin (*A*) (%, w/v)	Conc. of NVP (*B*) (%, w/v)	Conc. of APS (*C*) (mmol/L)	%GE (*Y*)
1	4 (+1)	1 (−1)	0 (−1)	19.75
2	3 (−1)	2 (+1)	10 (+1)	47.37
3	3 (−1)	1 (−1)	10 (+1)	2.90
4	4 (+1)	2 (+1)	0 (−1)	15.05
5	3 (−1)	1 (−1)	0 (−1)	0.9
6	4 (+1)	2 (+1)	10 (+1)	91.52
7	4 (+1)	1 (−1)	10 (+1)	23.91
8	3 (−1)	2 (+1)	0 (−1)	5.97

APS, ammonium persulfate; GE, grafting efficiency; NVP, N-vinyl pyrrolidone. Values in parenthesis indicate coded values.

2.6. Characterization of films of amylopectin and amylopectin-g-poly(N-vinyl-2-pyrrolidone)

The films of amylopectin and amylopectin-g-poly(N-vinyl-2-pyrrolidone) were characterized by scanning electron microscopy (SEM), swelling and *in vitro* release studies.

2.6.1. Swelling studies

Swelling properties of films were evaluated by determining their degree of swelling. Each film was cut into square pieces of (2 cm × 2 cm), weighed (W_0) and immersed in phosphate buffer of pH 1.2 and 6.8 in petri dishes (Perioli et al., 2004). At different time intervals, the films were carefully taken out and wiped with filter paper to remove the excess of surface water and weighed (W_t). The % swelling was calculated as follows:

$$\text{Swelling}\ \ (\%) = \frac{W_t - W_0}{W_0} \times 100 \qquad (2)$$

where W_0 is the initial weight of sample and W_t is weight at time '*t*'.

2.6.2. In vitro release study

The *in vitro* release of metronidazole from the prepared films was carried out in duplicate using USP type II apparatus (TDT-08L, Electrolab, Mumbai, India). The films were cut into a square of 3 cm × 3 cm (area of 9 cm^2) and adhered to glass slide with the aid of cyanoacrylate glue (Okamoto, Taguchi, Iida, & Danjo, 2001). The glass slides were then placed in the dissolution vessel filled with 200 ml of dissolution medium in such a way that the film was exposed to release media. The dissolution media comprised of phosphate buffer (pH 6.8) at 37.0 ± 0.5 °C and 50 rpm (Malik et al., 2012). An aliquot of 5 ml sample was withdrawn and replaced with another 5 ml of fresh dissolution media at various time intervals. The contents of metronidazole in withdrawn samples were determined by measuring absorbance at 320 nm in a UV–vis spectrophotometer (Cary 5000, Varian Australia).

3. Results and discussion

3.1. Synthesis and characterization of amylopectin-g-poly(N-vinyl-2-pyrrolidone)

Modification of properties of amylopectin was carried out by the graft polymerization of N-vinyl-2-pyrrolidone onto amylopectin using UV irradiation. Conventionally, graft co-polymerization of vinyl monomers onto natural polymers has been carried out using free-radical initiator-induced polymerization reactions. Amylopectin is a large molecule with pendant —OH groups and 1, 4-α-D-glucosidic linear linkages and 1,6-α-D-glucosidic linkages at the branched points. UV irradiation may result in cleavage of pendant O—H bonds of amylopectin molecule to form amylopectin macroradicals. The persulfate free radicals may also abstract hydrogen atom from amylopectin molecule to form these macroradicals. These free radicals further react with N-vinyl-2-pyrrolidone monomer to form N-vinyl-2-pyrrolidone free radicals, resulting in a series of free radical initiated chain reactions which ultimately terminate in formation of graft copolymer and homopolymer as shown below:

Chain initiation

$$S_2O_8^{2-} \rightarrow 2SO_4^{\bullet -}$$

$$AMOH + R^{\bullet} \xrightarrow{UV} AMO^{\bullet} + RH$$

where $R^{\bullet}$ is $SO_4^{\bullet -}$ and AMOH is amylopectin polysaccharide.

$$AMO^{\bullet} + N \rightarrow AMON^{\bullet}$$

$$R^{\bullet} + N \rightarrow RN^{\bullet}$$

where N is N-vinyl-2-pyrrolidone.

Chain propagation

$$AMON^{\bullet} + N \rightarrow AMON_1^{\bullet}$$

$$AMON_1^{\bullet} + N \rightarrow AMON_2^{\bullet}$$

$$AMON_{n-1}^{\bullet} + N \rightarrow AMON_n^{\bullet}$$

$$RN^{\bullet} + N \rightarrow RN_1^{\bullet}$$

$$RN_1^{\bullet} + N \rightarrow RN_2^{\bullet}$$

$$RN_{n-1}^{\bullet} + N \rightarrow RN_n^{\bullet}$$

Chain termination

$$AMON_n^{\bullet} + AMON_n^{\bullet} \rightarrow \text{graft co-polymer}$$

$$AMON_n^{\bullet} + RN_n^{\bullet} \rightarrow \text{graft co-polymer}$$

$$RN_n^{\bullet} + RN_m^{\bullet} \rightarrow \text{homopolymer}$$

The graft copolymer of amylopectin and NVP was characterized by FT-IR, DSC, X-ray diffractometry, and scanning electron microscopy (SEM). Fig. 1(a) represents the FTIR spectra of amylopectin and amylopectin-g-poly(N-vinyl pyrrolidone) in the frequency region of 4000–400 cm^{-1}. The spectra of amylopectin exhibits a characteristic broad peak at 3356 cm^{-1} and 3333 cm^{-1} attributed to —OH stretching band of hydroxyl group along with inter and intra-molecular H-bonding. Peak at 2932 cm^{-1} can be ascribed to C—H stretching of alkanes. C—H bending was confirmed by peaks at 926 cm^{-1}, 856 cm^{-1} and 764 cm^{-1}. The FT-IR spectra of amylopectin-g-poly(N-vinyl-2-pyrrolidone) showed variation in intensity and shifting of the peaks that appeared due to OH stretching indicating the participation of hydroxyl groups in chemical reaction. It shows a characteristic peak for C=O stretching vibration at 1620 cm^{-1} of cyclic amide (lactam), another peak at 1366 cm^{-1}

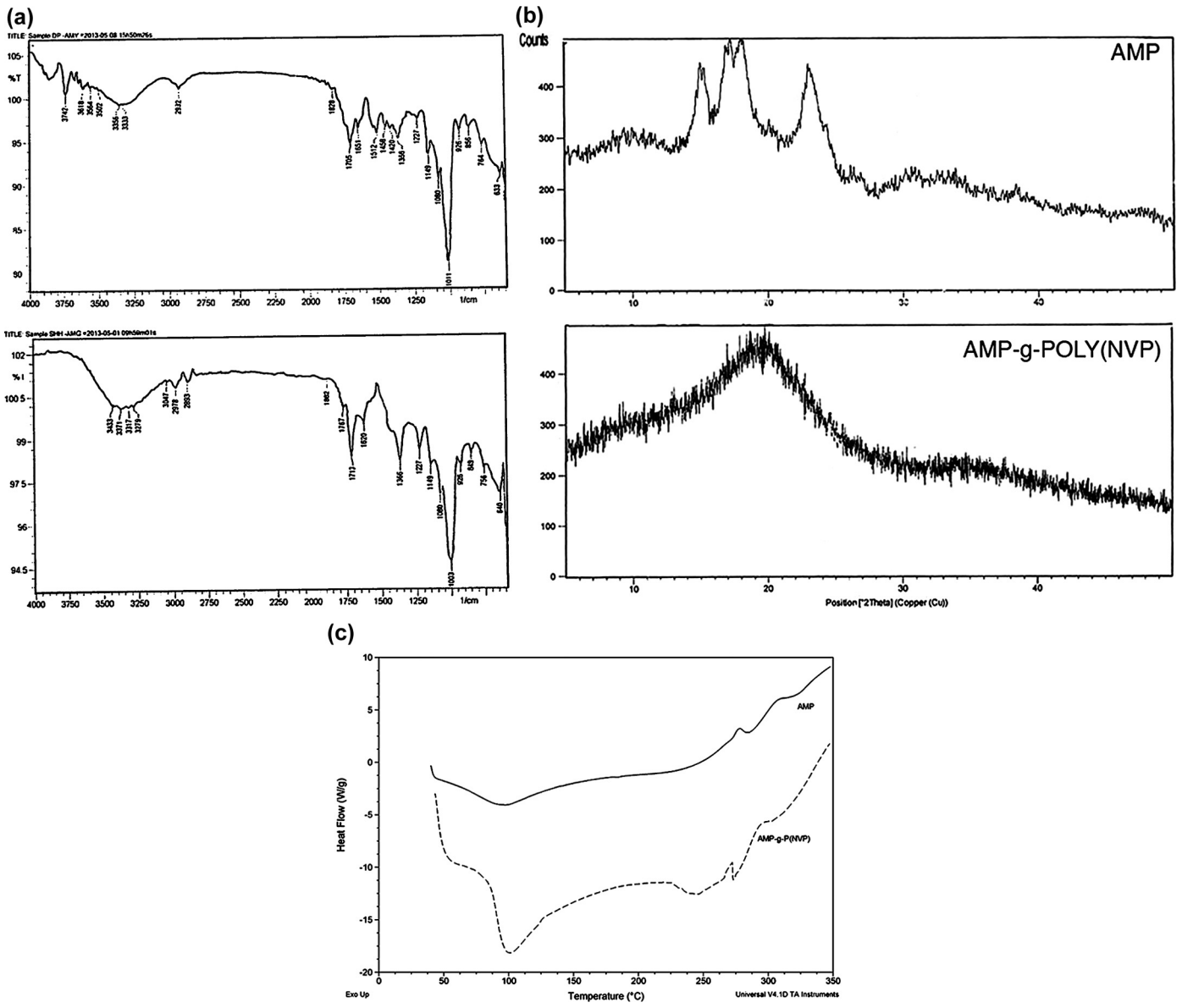

Fig. 1. (a) FT-IR spectra, (b) X-ray diffraction pattern and (c) thermal curves of amylopectin and amylopectin-g-poly(N-vinyl-2-pyrrolidone).

due to stretching of tertiary amine group which confirms the grafting of N-vinyl-2-pyrrolidone. Spectra shows an absorption band at 3433 cm^{-1} due to —OH stretching, a peak at 1080 cm^{-1} owing to —CO stretching of alcohol and another peak appearing at 2921 cm^{-1} due to —CH stretch of alkane group.

Fig. 1(b) represents the X-ray diffraction of amylopectin and amylopectin-g-poly(N-vinyl-2-pyrrolidone). The diffractogram of amylopectin shows characteristic peaks appearing at 15.12°, 17.03° and 22.97° (2θ) respectively. The diffraction pattern of amylopectin-g-poly(N-vinyl-2-pyrrolidone) shows a diffractogram in which the peaks are attenuated indicating the amorphous nature of graft copolymer.

Fig. 1(c) compares the thermal curves of amylopectin and amylopectin-g-poly(N-vinyl-2-pyrrolidone). The thermogram of amylopectin shows a broad endotherm at 97.54 °C followed by exotherm at 278.45 °C. The thermal curve of amylopectin-g-poly(N-vinyl-2-pyrrolidone) shows two endotherms at 98.80 °C and 240.36 °C followed by exotherm at 278.06 °C. Thus, appearance of endothermic peaks in the thermogram of graft copolymer indicates the modification of amylopectin.

Fig. 2 exhibits the scanning electron micrographs showing the shape and surface morphology of amylopectin and amylopectin-g-poly(N-vinyl-2-pyrrolidone). Amylopectin particles are polyhedral in shape (Fig. 2a) with surface bearing granular crystalline structures (Fig. 2b) while amylopectin-g-poly(N-vinyl-2-pyrrolidone) particles are cuboidal in shape (Fig. 2c) with relatively smooth surface (Fig. 2d). Thus, it can be observed that the grafting of amylopectin with NVP makes its surface smoother.

3.2. Effect of grafting conditions on grafting parameters

The concentration of amylopectin, concentration of N-vinyl pyrrolidone and the ammonium persulfate were selected as formulation variables, while % grafting efficiency (%GE) was chosen as the response variable for the optimization study. The optimization was carried out using three-factor, two level, full factorial experimental design. The results (Table 1) of grafting efficiency (%) of various batches of graft copolymer prepared using the experimental designs were subjected to factorial analysis using Design Expert software (Version 7.1.6, Stat-Ease, Inc., Minneapolis). On analysis,

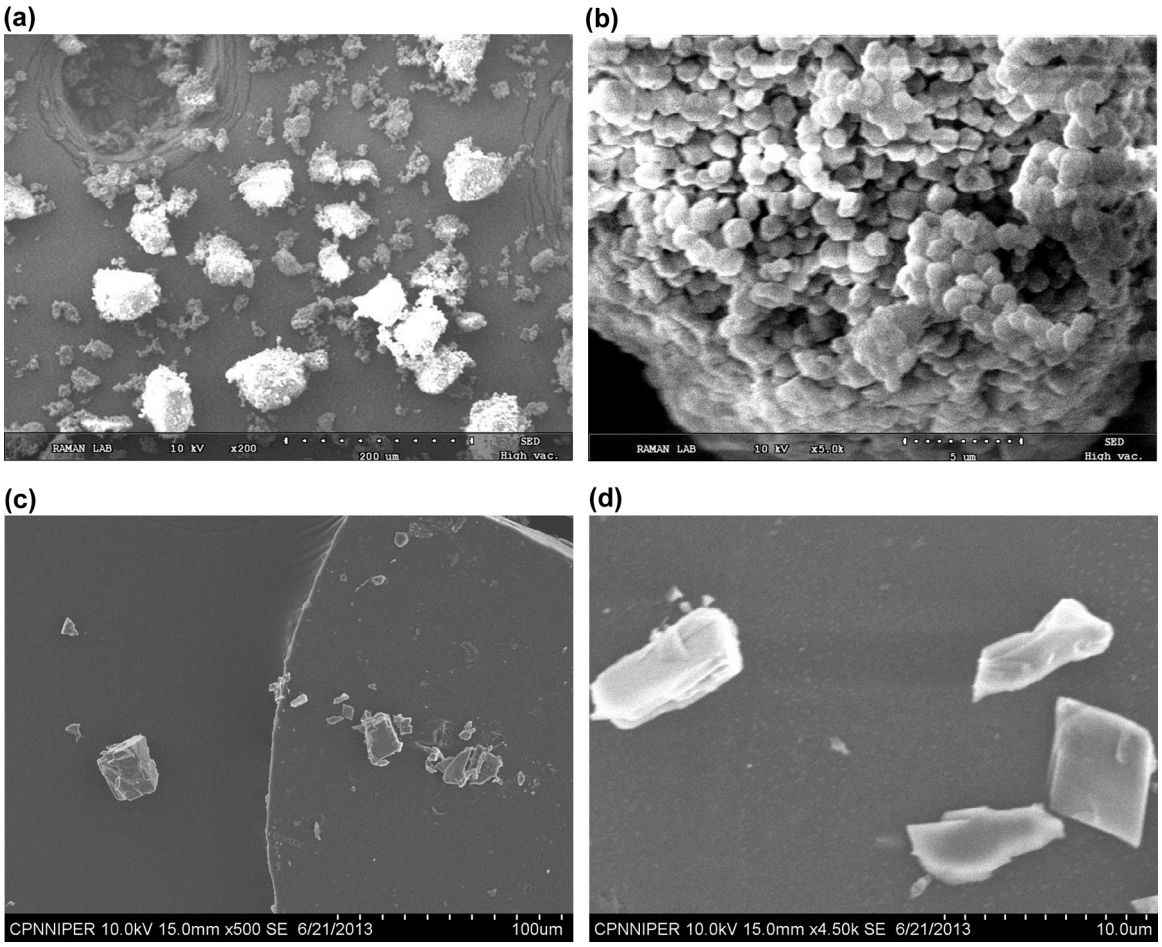

Fig. 2. Scanning electron micrographs showing (a) shape, (b) surface of amylopectin and (c) shape and (d) surface of amylopectin-g-poly(N-vinyl-2-pyrrolidone).

it was found that the response generated in the experiment on subjecting to square root transformation provided significant factorial model.

The factorial model describing the correlation between the independent variables and % grafting efficiency of graft copolymerization can be represented as:

$$\text{Sqrt}\ \ Y\ \ (\%) = 4.34 + 1.35 \times A + 1.35 \times B + 1.42 \times C - 0.32 \times A \times B + 1.12 \times B \times C \quad (3)$$

The results revealed that the grafting efficiency (%) was influenced significantly by the synergistic linear contribution of concentration of amylopectin (*A*), N-vinyl-2-pyrrolidone (*B*) and ammonium persulfate (*C*). The grafting efficiency was significantly affected by the synergistic interaction effects of *BC* while interaction effects of *AB* affected the grafting efficiency antagonistically.

The ANOVA analysis of the model revealed the model to be significant ($P < 0.05$). Further, the higher value of R^2 (0.9927) indicated a good correlation between the experimental and predicted response. In addition, the predicted R^2 value (0.8825) is in reasonably good agreement with adjusted R^2 value (0.9743), resulting in reliable model. Moreover, the higher value of adequate precision (20.887) indicates an adequate signal. The relatively lower value of coefficient of variance (10.47%) indicates better precision and reliability of the experiments carried out.

Fig. 3(a and b) depicts the combined effect of different variables on grafting efficiency. It can be observed from Fig. 3(a) that increasing the concentration of amylopectin and NVP results in an increase in grafting efficiency which may be ascribed to availability of greater amount of polymer matrix and vinyl monomers resulting in formation of greater amount of graft copolymer. Fig. 3(b) portrays the combined effect of concentration of NVP and ammonium persulfate on %GE. It is evident from the plot that at lower levels of NVP, concentration of APS has no effect on %GE but at higher levels of NVP increasing the concentration of APS results in an increase in %GE. This insignificant effect of APS at lower levels of NVP may be attributed to the formation of lesser vinyl radical due to inadequate vinyl monomer. However, on increasing the concentration of vinyl monomer, more free vinyl radicals are formed with increase in APS concentration leading to an increase in grafting efficiency.

A numerical optimization tool of design expert software, using the desirability approach was used to prepare the graft copolymer with the desired grafting. The optimization of independent variables was done with the goal of maximizing the %GE. The optimization tool provided us with a series of solutions. The solution with the highest desirability was selected for optimization study. The optimal calculated parameters were concentration of amylopectin (*A*) 4% (w/v), concentration of NVP (*B*) 2% (w/v) and concentration of APS 10 mmol/L. To validate the design model, optimal reaction and two additional checkpoint reactions in the design space were carried out. Table 2 details the test conditions of optimal and random checkpoints, their experimental and predicted values along with the calculated % prediction error. The lower values (−7.99 to 2.38) of % prediction error indicate robustness of the design model. The optimized batch of grafted copolymer has maximum %GE of 83.16.

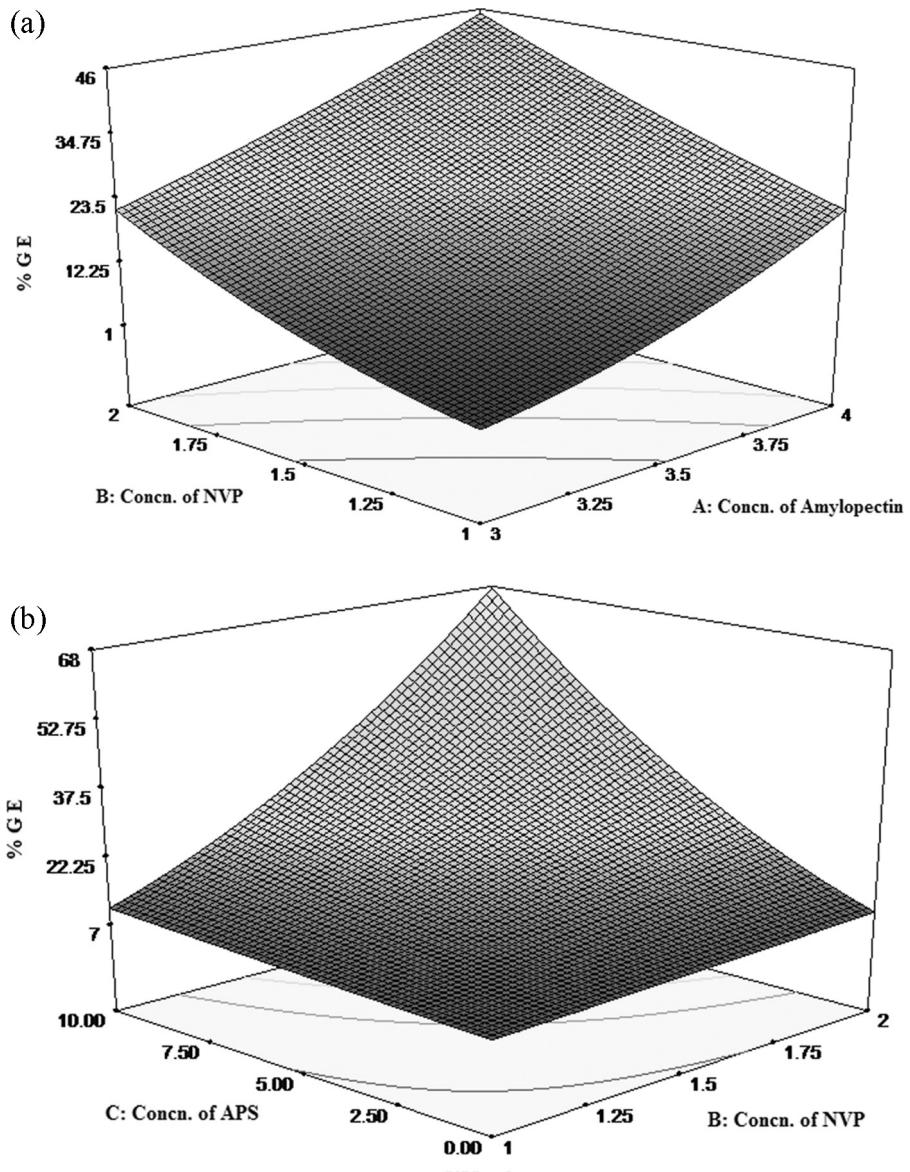

Fig. 3. Response surface plots showing the combined effect of concentrations of (a) amylopectin and NVP, (b) NVP and ammonium persulfate on the % grafting efficiency (GE).

3.3. *Amylopectin and amylopectin-g-poly(N-vinyl-2-pyrrolidone) films*

The optimized batch of amylopectin-g-poly(N-vinyl-2-pyrrolidone) was used to formulate films of metronidazole and compared with the films of amylopectin. The casted films were characterized by scanning electron microscopy (SEM) and further evaluated for swelling properties and *in vitro* release behavior. Fig. 4(a and b) exhibits the scanning electron micrographs showing the surface morphology of metronidazole loaded amylopectin and amylopectin-g-poly(N-vinyl-2-pyrrolidone) films. The surface of amylopectin films showed presence of crystalline structures while amylopectin-g-poly(N-vinyl-2-pyrrolidone) films showed porous and rougher surface.

The films were subjected to swelling studies at different pH values to ascertain whether grafting of NVP on amylopectin results in modification of the release properties of amylopectin. It can be observed from the results (Table 3) that grafting of NVP on amylopectin diminishes its swelling rate and extent. Further the films of amylopectin-g-poly(N-vinyl-2-pyrrolidone) kept at pH 1.2 and 6.8

Table 2
The experimental and predicted values for response *Y* along with percentage prediction error observed for the optimum test conditions and random checkpoints.

	Checkpoints conditions			% Grafting efficiency (*Y*)		
	A (%, w/v)	*B* (%, w/v)	*C* (mmol/L)	Observed	Predicted	Error (%)
1[a]	4	2	10	83.16	85.64	−2.98
2	3.5	2	10	60.45	65.28	−7.99
3	3.5	1.5	5	18.85	18.40	+2.38

[a] Optimum combination of a, amylopectin; b, NVP; c, ammonium persulfate.

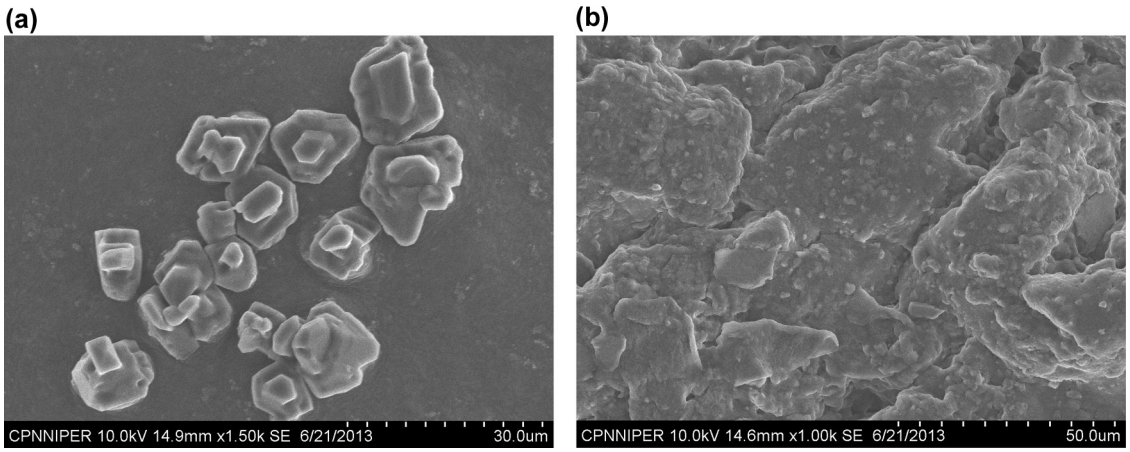

Fig. 4. Scanning electron micrographs of (a) amylopectin and (b) amylopectin-g-poly(N-vinyl-2-pyrrolidone) film.

Table 3
Swelling of amylopectin and amylopectin-g-poly(N-vinyl-2-pyrrolidone) films at different pH.

Time (min)	% Swelling[a]			
	Amylopectin film		Amylopectin-g-poly(N-vinyl-2-pyrrolidone) film	
	pH 1.2	pH 6.8	pH 1.2	pH 6.8
15	22.20 ± 0.98	20.80 ± 0.56	10.20 ± 0.21	15.20 ± 0.25
30	39.62 ± 0.67	35.60 ± 0.28	21.20 ± 0.42	22.40 ± 0.28
60	61.18 ± 1.72	50.80 ± 0.84	19.28 ± 0.39	37.40 ± 0.09
120	90.35 ± 0.07	66.40 ± 1.27	28.69 ± 0.17	44.60 ± 1.13
180	34.79 ± 0.21	83.72 ± 0.28	55.56 ± 1.21	52.20 ± 0.56
240	−14.32 ± 0.50	33.41 ± 0.42	58.95 ± 0.63	59.00 ± 1.41
300	−67.19 ± 1.13	15.59 ± 0.07	21.20 ± 0.28	69.40 ± 0.56
360	–	−28.39 ± 0.26	−32.50 ± 0.21	46.20 ± 0.28
420	–	−79.61 ± 0.14	−75.84 ± 0.62	−7.80 ± 0.10

[a] Values are mean ± SD ($n = 3$).

started eroding at 4 and 5 h respectively compared to amylopectin films which began eroding after 2 and 3 h respectively. Thus, the slower swelling and erosion of amylopectin-g-poly(N-vinyl-2-pyrrolidone) indicated its usefulness to sustain the release rate. Thus, amylopectin-g-poly(N-vinyl-2-pyrrolidone) films containing metronidazole were formulated for sustained release applications. Fig. 5 shows the *in vitro* release profile of metronidazole from the amylopectin and amylopectin-g-poly(N-vinyl-2-pyrrolidone) films. It can be observed that amylopectin films release almost all the drug in 5 h while amylopectin-g-poly(N-vinyl-2-pyrrolidone) showed a prolonged release over 7 h.

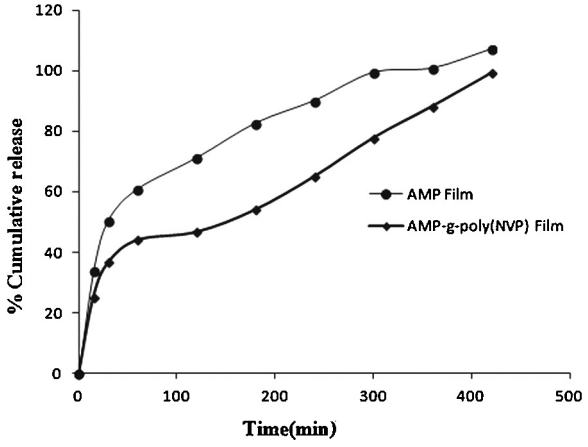

Fig. 5. *In vitro* release profile of metronidazole from amylopectin and amylopectin-g-poly(N-vinyl-2-pyrrolidone) films.

To further investigate the mechanism of drug release, the data was subjected to modeling and release kinetics. The respective values of R^2 and K for various kinetic models for amylopectin films were 0.803 and 0.2006% h^{-1}(zero-order), 0.8477 and 0.0133 h^{-1}(first-order), 0.9538 and 4.808% $h^{-0.5}$ (Higuchi square root), while the corresponding values of R^2 and K for amylopectin-g-poly(N-vinyl pyrrolidone) films were 0.913 and 0.1025% h^{-1}(zero-order), 0.9171 and 0.0039 h^{-1}(first-order), 0.9599 and 4.2471% $h^{-0.5}$ (Higuchi square root). The results thus reveal that the release of drug from films fitted best into Higuchi square kinetics (Costa & Sousa, 2001). Further, the value of 'n' the release exponent of Korsmeyer–Peppas for amylopectin and amylopectin-g-poly(N-vinyl pyrrolidone) films was found to be 0.695 and 0.671 respectively, indicating ($0.45 \leq n \leq 0.89$) that the films released the drug by combination of diffusion through the matrix and matrix erosion (Siepmann & Peppas, 2001). The release rate of the drug from film matrices depends upon a number of factors such as concentration of drug, polymer and plasticizer. By varying the concentration of different formulation variables one can achieve the desired release rate.

4. Conclusion

The graft co-polymerization of N-vinyl-2-pyrrolidone on amylopectin was optimized using 2-level, 3-factor full factorial experimental design. The results revealed that the concentrations of amylopectin, NVP and ammonium persulfate had a significant synergistic effect on the grafting efficiency. The graft co-polymer was further characterized by FT-IR, DSC, XRD, and SEM analysis that confirmed the formation of

amylopectin-g-poly(N-vinyl-2-pyrrolidone). In addition, the graft co-polymer was evaluated for modification of release rate employing films of metronidazole. The study revealed a prolonged release of metronidazole from graft copolymer films as compared with amylopectin. Thus on the basis of results of the present study it can be concluded that grafting of N-vinyl-2-pyrrolidone on amylopectin prolongs the drug release However, further systematically designed optimization studies are needed to further comment on this. Thus, UV assisted graft co-polymerization can be used as an efficient tool to modify the release properties of amylopectin by grafting of NVP on amylopectin. The promising prolonged release properties of amylopectin-g-poly(N-vinyl-2-pyrrolidone) warrants its further exploration in formulation of pharmaceutical dosage forms.

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References

Ausman, K. D., Smalley, R. E., O'Connell, M. J., Boul, P. J., Ericson, L. M., & Huffman, C. B. (2001). Reversible water-solubilization of single walled carbon nanotubes by polymer wrapping. *Chemical Physics Letters*, *342*, 265–271.

Bhattacharya, A., & Misra, B. N. (2004). Grafting: A versatile means to modify polymers-technique, factors and application. *Progress in Polymer Sciences*, *29*, 767–814.

Costa, P., & Sousa, L. J. M. (2001). Modeling and comparison of dissolution profiles. *European Journal of Pharmaceutical Sciences*, *13*, 123–133.

El-Kamel, A. H., Ashri, L. Y., & Alsarra, I. A. (2007). Micromatricial metronidazole benzoate film as a local mucoadhesive delivery system for treatment of periodontal diseases. *AAPS PharmSciTech*, *8*(3). Article 75.

Fanta, G. F., & Doane, W. M. (1986). In O. B. Wurzburg (Ed.), *Modified starches: Properties and uses*. Boca Raton, FL: CRC Press.

Kumar, A., Singh, K., & Ahuja, M. (2009). Xanthan-g-poly(acrylamide): Microwave-assisted synthesis, characterization and *in vitro* release behavior. *Carbohydrate Polymers*, *76*, 261–267.

Lee, J. W., Park, J. H., & Robinson, J. R. (2000). Bioadhesive-based dosage forms: The next generation. *Journal of Pharmaceutical Sciences*, *89*, 850–866.

Malik, S., Kumar, A., & Ahuja, M. (2012). Synthesis of gum kondagogu-g-poly(N-vinyl-2-pyrrolidone) and its evaluation as a mucoadhesive polymer. *International Journal of Biological Macromolecules*, *51*, 756–762.

Malik, S., & Ahuja, M. (2011). Gum kondagogu-g-poly (acrylamide): Microwave-assisted synthesis, characterisation and release behavior. *Carbohydrate Polymers*, *86*, 177–184.

Mishra, M. M., Yadav, M., Mishra, D. K., & Behari, K. (2011). Synthesis of graft co-polymer (CmgOH-g-NVP) and study of physicochemical properties: Characterization and application. *Carbohydrate Polymers*, *83*(4), 1749–1756.

Nabais, T., Brouillet, F., Kyriacos, S., Mroueh, M., Amores da Silva, P., Bataille, B., et al. (2007). High-amylose carboxymethyl starch matrices for oral sustained drug-release: In vitro and in vivo evaluation. *European Journal of Pharmaceutics and Biopharmaceutics*, *65*, 371–378.

Nho, Y. C., & Park, K. R. (2002). Preparation of properties of PVA/PVP hydrogel containing chitosan by radiation. *Journal of Applied Polymer Science*, *85*, 1787–1794.

Nud'ga, L. A., Petrova, V. A., Klishevich, N. V., Litinova, L. S., Babenko, A., & Shelegedin, V. N. (2002). Synthesis and microbiological stability of graft co-polymers of NVP and chitosan. *Russian Journal of Applied Chemistry*, *75*, 1678–1682.

Okamoto, H., Taguchi, H., Iida, K., & Danjo, K. (2001). Development of polymer film dosage forms of lidocaine for buccal administration. *Journal of Controlled Release*, *77*, 253–260.

Perioli, L., Ambrogi, V., Angelici, F., Ricci, M., Giovagnoli, S., Capuccella, M., et al. (2004). Development of mucoadhesive patches for buccal administration of ibuprofen. *Journal of Controlled Release*, *99*, 73–82.

Phillips, G. O. (1980). In W. W. Pigman, & D. Horton (Eds.), *The carbohydrate: Chemistry and biochemistry*. New York: Academic Press.

Rana, V., Rai, P., Tiwary, A. K., Singh, R. S., Kennedy, J. F., & Knill, C. J. (2011). Modified gums: Approaches and applications in drug delivery. *Carbohydrate Polymers*, *83*, 1031–1047.

Rindlav-Westling, A., Stading, M., Hermansson, A.-M., & Gatenholm, P. (1998). Structure, mechanical and barrier properties of amylase and amylopectin films. *Carbohydrate Polymers*, *36*, 217–224.

Sand, A. M., Mishra, D. K., & Behari, K. (2010). Modification of alginate by grafting of N-vinyl-2-pyrrolidone and studies of physicochemical properties in terms of swelling, metal-ion uptake and flocculation. *Carbohydrate Polymers*, *80*, 1147–1154.

Sarkar, A., Mandre, N. R., Panda, A. B., & Pal, S. (2013). Amylopectin grafted with poly(acrylic acid): Development and application of a high performance flocculant. *Carbohydrate Polymers*, *95*, 753–759.

Sen, G., Kumar, R., Ghosh, S., & Pal, S. (2009). A novel polymeric flocculant based on polyacrylamide grafted carboxymethyl starch. *Carbohydrate Polymers*, *77*, 822–831.

Siepmann, J., & Peppas, N. A. (2001). Modeling of drug release from delivery system based on hydroxypropyl methylcelloluse. *Advanced Drug Delivery Reviews*, *48*, 139–157.

Singh, V., Tiwari, A., Tripathi, D. N., & Sanghi, R. (2006). Microwave enhanced synthesis of chitosan-*graft*-polyacrylamide. *Polymer*, *47*, 254–260.

Singh, V., Tiwari, A., Tripathi, D. N., & Sanghi, R. (2004). Microwave assisted synthesis of guar-g-polyacrylamide. *Carbohydrate Polymers*, *58*, 1–6.

Singh, R. P., Nayak, B. R., Biswal, D. R., Tripathy, T., & Banik, K. (2003). Biobased polymeric flocculants for industrial effluent treatment. *Material Research Innovation Journal*, *7*, 331–340.

Singh, R. P., Pal, S., Rana, V. K., & Ghorai, S. (2013). Amphoteric amylopectin: A novel polymeric flocculant. *Carbohydrate Polymers*, *91*, 294–299.