IVABRADINE HYDROCHLORIDE DIRECTLY COMPRESSED TABLETS USING NANO-CELLULOSE EXTRACTED FROM *ARACHIS HYPOGAEA* SHELLS

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ABSTRACT

Objective: The main objective of this work was the extraction of nanocellulose from *Arachis hypogaea* shells, characterization of nanocellulose, development, and *in vitro* evaluation of directly compressed tablets of ivabradine hydrochloride (IVH) using nanocellulose.

Methods: IVH and colloidal silicon dioxide are gift samples from Mylan Laboratory, Hyderabad, and Karnataka Antibiotics and Pharmaceuticals Ltd., Bengaluru, respectively. Nanocellulose was extracted from *A. hypogaea* shells by alkaline treatment followed by acid hydrolysis and it was characterized by particle size analysis by zeta sizer, melting point determination, differential scanning calorimetry (DSC), and Fourier transform infrared (FTIR) analysis. Compatibility between IVH and nanocellulose was confirmed by FTIR and DSC analysis. Then, fast-release tablets of containing 5 mg of IVH were prepared by direct compression using various compositions containing nanocellulose, starch, and colloidal silicon dioxide and evaluated.

Results: Nanocellulose in the size of 273.4 nm was extracted from *A. hypogaea* shells to possess its ideal characteristics. IVH and nanocellulose were compatible according to FTIR and DSC analysis. Fast-release tablets of IVH were prepared as directly compressed tablets by direct compression. Tablets made with 5 mg of IVH and nanocellulose, starch, and colloidal silicon dioxide evidenced fast release of 96.37% in 5 min.

Conclusion: Nanocellulose from *A. hypogaea* shells can be produced successfully by alkali treatment followed by acid hydrolysis, ball milling, and lyophilization. This nanocellulose can be exploited successfully for the design of fast-release tablets of IVH.

Keywords: Nanocellulose, *Arachis hypogaea* shells, Soxhlation method, Fourier transform infrared, Compatibility, Ivabradine hydrochloride, Fast release.

INTRODUCTION

Pharmaceutical excipients play a key role in formulation development of therapeutics. Synthetic polymers and celluloses are exploited for the production of directly compressed vehicle to produce tablets without granulation due to their reported compatibility. Especially, naturally occurring celluloses are studied as pharmaceutical excipients due to their compressibility, low toxicity, biodegradability, and renewable nature [1]. It was reported that all-cellulose composites possess an intriguing combination of high strength and biodegradability [2]. Cellulose is listed as a direct compression vehicle to produce tablets by direct compression without granulation procedures. This saves lots of economy on the part of the manufacturing productions. Hence, in an attempt in an advanced study in this line, we have selected to evaluate nanocellulose to produce tablets by direct compression.

The advanced product called nanocellulose is further processed nanosized cellulose fibrils with a very high aspect ratio. Typically, lateral dimensions are 5–20 nm and longitudinal dimensions are in a wide range, typically several micrometers. Nanocellulose can be extracted from plant cell wall and can be extracted from a variety of sources, such as wood, bast fibers, grasses, seed fibers, marine animals, algae, fungi, invertebrates, and bacteria [3]. India, being an agricultural country, generates mind-boggling amount of agricultural waste, which is over 320 million tons per year. Main sources of agro-waste are paddy straw, sugarcane biogases, peanut shells, coffee husk, and maize husk.

Therefore, in the present work, *Arachis hypogaea* (peanuts) have been selected for extraction of nanocellulose from it and ivabradine hydrochloride (IVH) was selected as a model drug to exploit nanocellulose for the design of directly compressed tablets of IVH.

IVH is a new drug approved by the United States Food and Drug Administration in April 2015 for the treatment of chronic stable angina pectoris in coronary artery disease. The nature of nanocellulose is expected to produce compact tablet with fast release as there may be a need for quick therapeutic effect for the treatment of angina pectoris. IVH is generally used in adult patients who do not tolerate or cannot take heart medicines called beta-blockers.

MATERIALS AND METHODS

Materials
IVH and colloidal silicon dioxide are gift samples from Mylan Laboratory, Hyderabad, and Karnataka Antibiotics and Pharmaceuticals Ltd., Bengaluru, respectively. Urea nitric acid was purchased from SD Fine Chemical Laboratories. All other chemicals used in the study are of analytical grade.

Methods
Various stages of the present research include extraction of nanocellulose from *A. hypogaea* shells, characterization, development of fast-release tablets of IVH, and *in vitro* evaluation of prepared tablets.

Isolation of nanocellulose
A. hypogaea shells were collected from local peanut mill (Tirupati, Chittoor district, Andhra Pradesh). They were washed with water to remove the soil contents and then sundried for 5 days to remove moisture content. The dried shells were ground into fine powder using a mill and were sieved using sieve no. 120 [4].

Thirty grams of the powder were treated with 800 ml of 0.5 M NaOH for 3 h at 90°C with continuous stirring. The obtained dark slurry was

filtered and then washed several times with distilled water and then dried. The dried powder was again ground into a fine powder using a mill. Milled powder was refluxed with a mixture containing 30% (v/v) of nitric acid in ethanol. After this treatment, the color of the powder changed from light red to yellow in color. This residue was until the constant weight is obtained. The dried powder was again subjected to grinding in ball mill for 20 min and further kept for drying in a lyophilizer (Lyodel, Japan) for 24 h. Fig. 1 shows images of the product obtained at various stages of extraction. This yield was stored in polyethylene bags for characterization [5,6].

Characterization of nanocellulose

Percentage yield

The percentage yield of cellulose was calculated by the percentage ratio of actual yield to theoretical yield [7].

$$\% \text{ yield of cellulose} = \frac{W2}{W1} \times 100$$

Where,

W_2 is the weight of the resultant cellulose and
W_1 is the initial weight of peanut shell powder.

Determination of particle size by zeta sizer

Particle size of cellulose was determined using zeta sizer (Horiba). One milligram of sample was weighed and suspended in 5 ml of distilled water. This liquid sample was taken in 1 cm cuvettes and the particle size and zeta potential were determined [8].

Determination of moisture content

Grounded powder, 3 g was weighed accurately in a dry Petri dish and dried at 105°C for 6 h. The sample was allowed to cool, reweighed the sample and weight of sample was recorded [9,10]. The procedure was repeated until the weight of sample was constant. The moisture content was measured using the following equation:

$$\text{Moisture content} \ (\%) = \frac{W1 - W2}{W1} \times 100$$

Fig. 1: Various stages and images during the extraction of nanocellulose from *Arachis hypogaea* shells

Where,
W_1 is the initial weight of peanut shells powder and
W_2 is the final weight of peanut shell powder.

Determination of ash content

Crucible was weighed accurately (W1 g). About 2 g of peanut shell powder was weighed accurately along with crucible ($W_{2 g}$). The sample was used with the help of muffle furnace at 600°C for 6 h, cooled the crucible for ½h, and weighed the ash containing crucible (W_3). The ash content is calculated using the following formula [11,12]:

$$\text{Ash content} \ (\%) = \frac{W3 - W1}{W2 - W1} \times 100$$

Where, W_1 was the weight of crucible
W_2 was the weight of peanut shell powder and crucible and
W_3 was the weight of ash and crucible.

Determination of melting point

The melting point of prepared nanocellulose sample was determined by open capillary tube method.

Solubility of nanocellulose

Cellulose is insoluble in water and it was reported that it is soluble in 10% NaOH and 12% urea in water. Hence, in the present study, the prepared nanocellulose (4%) was dissolved in water containing 7% NaOH and 12% urea. After 10 min of vigorous stirring, the suspension of cellulose and solvent was cooled to −10°C and stirring was continued for 1 h for complete solubility [2].

Fourier-transform infrared (FTIR) spectroscopy of cellulose

The chemical constituents of nanocellulose were investigated by FTIR spectroscopy (Bruker, Japan). Sample was prepared by a pressed pellet technique. The FTIR spectrum of the nanocellulose was recorded in transmittance mode in the range of 400–4000 cm^{-1}.

Differential scanning calorimetry (DSC) of nanocellulose

DSC analysis of nanocellulose was carried out using DSC analyzer (Mettler Toledo, Switzerland). Heat flow rate was 10°C/min and sample was heated from 200°C to 400°C to detect possible interaction of polymer [13].

Interaction studies between IVH and nanocellulose

To assess compatibility between IVH and cellulose extracted from peanut shells, FTIR spectra and DSC thermogram were obtained for pure IVH and a 1:1 1 mixture of IVH and nanocellulose and investigated for interaction.

Development of directly compressed tablets of IVH using nanocellulose

As there is no interaction between IVH and nanocellulose of *A. hypogaea* shells, tablets containing 5 mg of IVH were prepared by direct compression using this nanocellulose as the main vehicle to produce tablets without the use of granulating agents. Eight formulations F1–F8 were tried and their composition is given in Table 1. The ingredients are weighed accurately and mixed uniformly using mortar and pestle and later to obtain a uniform mix of all the ingredients. The mixtures are evaluated for pre-compression characteristics. As they are satisfactory, they were compressed into tablets using 9 mm single punch tablet machine.

Evaluation of pre-compression characteristics

Pre-compression characteristics of powder of formulations F1–F8 were assessed by the determination of compressibility index, angle of repose, and Hausner's ratio.

Compressibility index and Hausner's ratio

Powdered mixture of 10 g was taken in a 100 ml measuring cylinder. The volume of the powder was noted (bulk volume). The cylinder was

Table 1: Formulation of ivabradine hydrochloride directly compressed tablets

Formulation	IVH (mg)	Colloidal silicon dioxide (mg)	Nanocellulose (mg)	Starch (mg)
F1	5	10	165	10
F2	5	10	170	5
F3	5	20	155	15
F4	5	10	180	5
F5	5	25	135	10
F6	5	10	180	5
F7	5	20	170	5
F8	5	30	150	15

IVH: Ivabradine hydrochloride

subjected to a fixed number of taps (100). Then, the final volume of the powder was recorded (tapped volume). Then, the bulk density, true density, compressibility index, and Hausner's ratio were calculated using the following equation:

$$\text{Bulk density} = \frac{\text{Weight of the powder}}{\text{Bulk volume}}$$

$$\text{Tapped density} = \frac{\text{Weight of the powder}}{\text{Tapped volume}}$$

$$\text{Compressibility index} = \frac{\text{Tapped density} - \text{Bulk density}}{\text{Tapped volume}} \times 100$$

$$\text{Hausner's ratio} = \frac{\text{Tapped density}}{\text{Bulk volume}}$$

Angle of repose
Using a fixed height funnel method, the angle of repose was calculated. The funnel height was kept constant 2 cm (h) and the diameter (D) of the circle was measured and the angle of repose was find out using the following equation:

$$\theta = \tan^{-1}\frac{h}{r}$$

Where,
h = height of the cone
r = radius of the base.

Evaluation of prepared directly compressed tablets
The following evaluation tests were performed for the tablets: Weight variation test, hardness, drug content, friability, disintegration test, and dissolution rate testing.

Weight variation test
Weight variation was calculated as per the method described in I. P [14]. Twenty tablets were selected at random and their average weight was determined. The tablets were weighed individually and compared with average weight to assess acceptance criteria as per official criteria as given below.

Average weight of tablet (mg)	Percentage difference allowed
80 or less	±10
80–250	±7.5
>250	±5

Hardness test
The hardness of tablets was measured using the Monsanto hardness tester.

Thickness
The thickness of tablets was determined using a digital Vernier caliper.

Drug content
The tablet was taken in a mortar and pestle, it was made into powder and transferred into a 100 ml volumetric flask and made up to the mark with 6.8 phosphate buffer. This solution was estimated for drug content by an ultraviolet spectrophotometer at 286 nm.

Friability test
A pre-weighed 10 tablets were placed in the Friabilator (Veego Instruments Ltd., India) which is then operated for 100 revolutions. The tablets were dusted and reweighed again.

$$\text{Friability} = (W1-W2)/W1 \times 100$$

Where,
Weight of 10 tablets = W1
Weight of 10 tablets after friability = W2.

Disintegration test
Disintegration test was carried out using disintegration test apparatus (Thermionic, India). Randomly selected six tablets were placed into a testing basket assembly, which is introduced into a special holder and placed into a water bath. The water inside the water bath is heated to 37°C±0.5°C. The basket assembly was moved smoothly up and down for 28–32 stokes/min and for a distance of 55 mm. The samples are disintegrated if no solid rest is left within the basket. The time taken for the tablets to disintegrate was noted.

***In vitro* drug release studies**
In vitro drug release studies were conducted for prepared tablets F1–F8 which were using USP dissolution testing apparatus, Type II (Electrolab, India) [15]. The dissolution medium was 900 ml of pH 6.8 phosphate buffer maintained at a temperature of 37°C±0.5°C. The paddle was rotated at a speed of 50 rpm. At specific time intervals, 5 ml aliquot samples were withdrawn and were replaced with fresh dissolution medium to maintain sink conditions. The samples were suitably diluted wherever necessary and estimated for IVH content by measuring the absorbance at 286 nm using UV spectrophotometer (Shimadzu). The test was also conducted for commercial tablets of IVH for comparison purpose.

Drug release kinetics
To study the release kinetics, data obtained from *in vitro* dissolution studies were fitted to various kinetic models such as zero-order, first-order, Higuchi model, and Korsmeyer–Peppas model.

RESULTS AND DISCUSSION

Nanocellulose extracted was in light yellowish color with a characteristic odor. It was assessed for its characteristics such as percentage moisture content, percentage ash content, percentage yield, melting point, solubility, particle size determination, FTIR spectrophotometer, and DSC to access its use in design of directly compressed tablets of IVH.

Percentage yield
The sequential treatment of peanut shells powder with NaOH, 25% nitric acid in ethanol resulted in dissolution or degradation of proteins and lignin. Yielding of extracted nanocellulose was 35%. In general, the nanocellulose content present in the peanut shells was 37%. Hence,
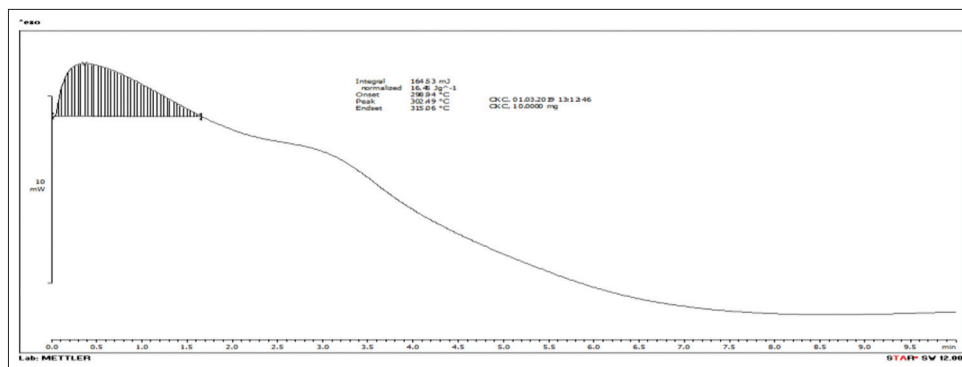
Fig. 2: Differential scanning calorimetry thermogram of nanocellulose
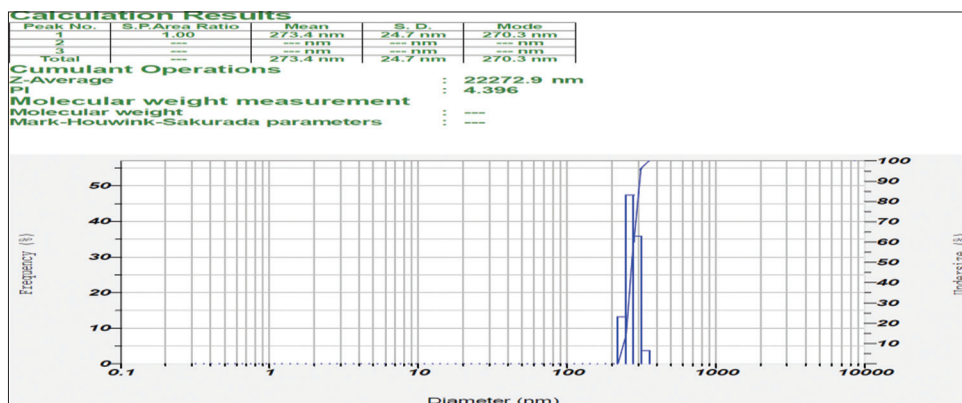

Fig. 3: Particle size of nanocellulose of *Arachis hypogaea* shells

the obtained percentage yield of nanocellulose was within the range as compared with reference value [2].

Particle size determination of nanocellulose
The scan of particle size analysis obtained from zeta sizer, as shown in Fig. 2. As indicated in Fig. 3, the mean particle size of the prepared nanocellulose is 273.4 nm. This indicates that the present method used for isolation of nanocellulose is successful in producing cellulose in nanosize.

Percentage moisture content
The percentage moisture content of nanocellulose was found to be 4.38%. This value below 10% indicates its good shelf-life, usability, and quality [2].

Percentage ash content
The percentage ash content of nanocellulose was found to be 0.1%. The ash content of the peanut nanocellulose was reported to be below 5%. This indicates the prepared nanocellulose having reasonable value of ash content.

Melting point
The melting point of the isolated nanocellulose was found to be 316.49°C and is coinciding with the reported melting point of cellulose, i.e., 316°C [2].

Solubility of nanocellulose
It was observed that the prepared nanocellulose was completely dissolved in 10% NaOH and 12% urea.

FTIR spectroscopy of nanocellulose
FTIR spectrum of extracted nanocellulose is shown in Fig. 4. It revealed its OH stretching vibration at 3341 cm^{-1} and C-H stretching vibrations at 2911 cm^{-1} and 1643 cm^{-1}. The data coincide with reported IR absorption peaks, as shown in Table 2, confirm the structural conformity of the prepared nanocellulose.

Table 2: Infrared absorption peaks of nanocellulose

Functional group	Reported (cm^{-1})	Obtained (cm^{-1})
O-H stretching	3400	3341
C-H stretching	2900 and 1627	2911 and 1643

Table 3: Data for Fourier transform infrared of IVH and mixture of IVH and nanocellulose

Functional group	Pure IVH (cm^{-1})	IVH with nanocellulose
O-CH3 stretching	1250 and 1059	1250 and 1061
C=O stretching	1656	1651
C=C stretching	1520	1519
C-N stretching of tertiary aliphatic amine	1059	1061
Symmetric C-H stretching	2947	2947
Stretching N-H	3475	3482

IVH: Ivabradine hydrochloride

DSC of nanocellulose
DSC thermogram of nanocellulose of peanut shells is shown in Fig. 5. As revealed in thermogram typical with onset temperature of decomposition was started just above 300°C and then with endothermic peak was present at 302.49°C. This coincides with the behavior of nanocellulose reported for peanut shells.

Interaction studies between IVH and nanocellulose
To assess the compatibility between IVH and cellulose extracted from peanut shells, FTIR spectra and DSC thermogram were obtained for pure IVH and a 1:1 1 mixture of IVH and nanocellulose.

FTIR spectra of IVH and mixture of IVH and NC are shown in Figs. 6 and 7. The data of peaks are summarized in Table 3. It is evident that all
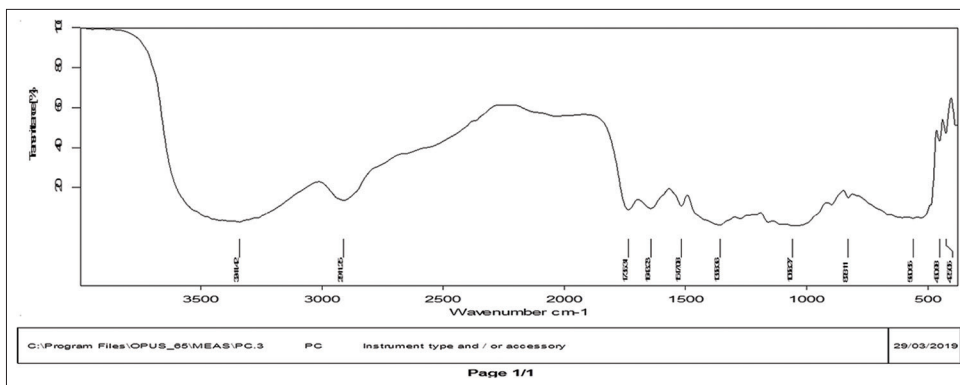
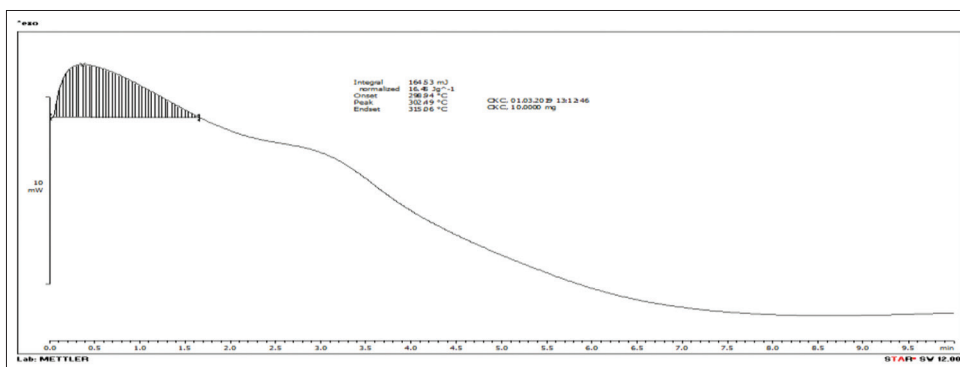**Fig. 4: Fourier-transform infrared spectroscopy of nanocellulose**

Fig. 5: Differential scanning calorimetry thermogram of nanocellulose
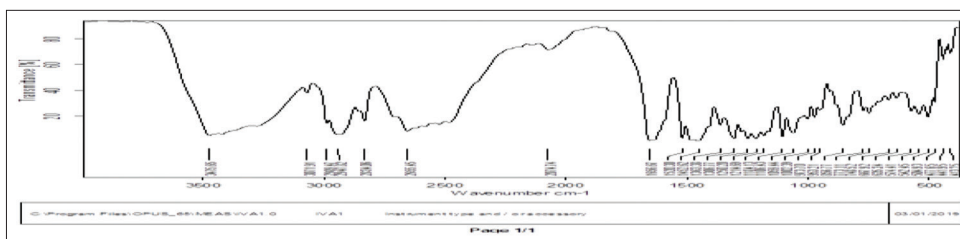

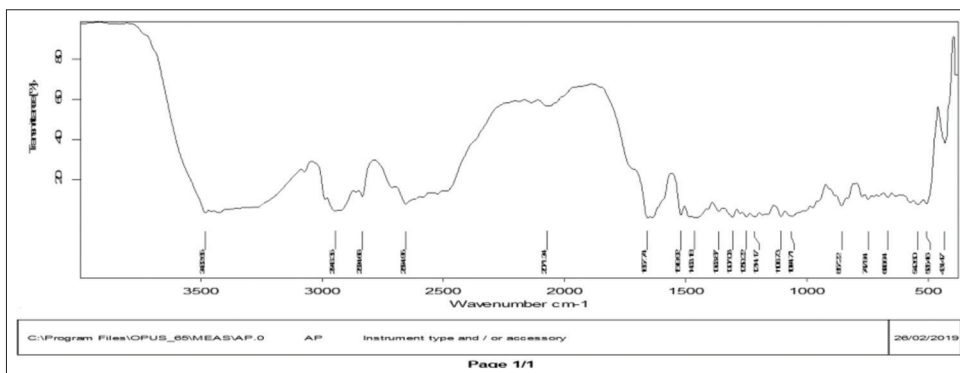**Fig. 6: Fourier transform infrared spectra of ivabradine hydrochloride**

Fig. 7: Fourier transform infrared spectrum of ivabradine hydrochloride and nanocellulose mixture

the absorption peaks of main functional groups of IVH are present on mixing with prepared nanocellulose indicating no interaction.

DSC thermogram in Fig. 8 showed sharp endotherm of IVH at 198.17°C. DSC thermogram of nanocellulose in Fig. 2 revealed its melting point peak at 302.49°C. DSC thermogram of mixture of IVH and NC in Fig. 9 exhibits melting peaks at 190°C and 308°C corresponding to IVH and

NC. These results indicate that there is no drug excipient interaction between IVH and NC.

Evaluation of pre-compressed characteristics
The results of pre-compression characteristics of IVH tablets F1–F8 are given in Table 4. As shown in table, the angle of repose values ranging from 21.80° to 30.96°, compressibility index from 9% to 20%, and
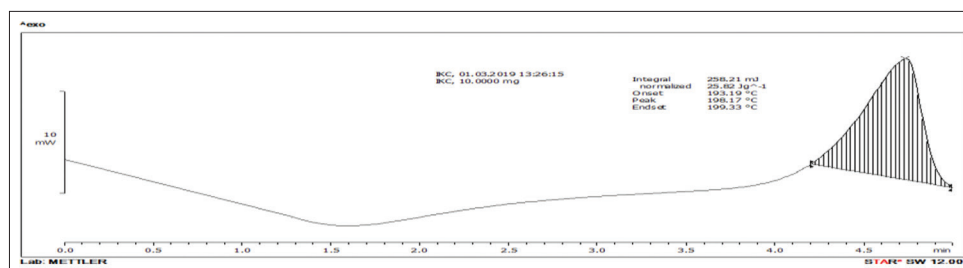
Fig. 8: Differential scanning calorimetry graph of ivabradine hydrochloride
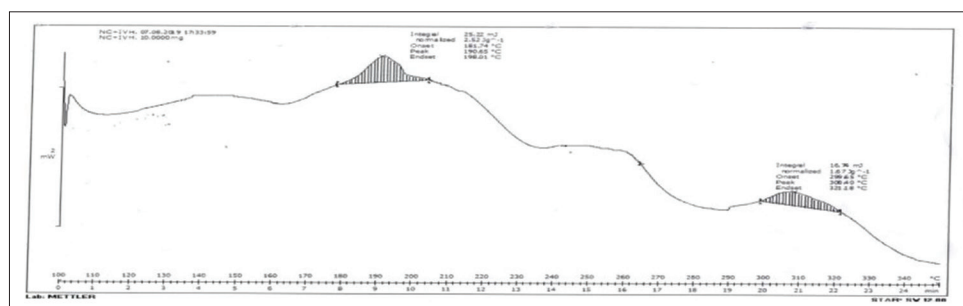

Fig. 9: Differential scanning calorimetry thermogram of ivabradine hydrochloride and nanocellulose

Table 4: Pre-compression characteristics of IVH tablets F1–F8

Formulation code	Angle of repose (θ)	Bulk density (g/cm³)	Tapped density (g/cm³)	Compressibility index (%)	Hausner's ratio
F1	30.8±0.2	0.166±0.001	0.2±0.008	17±0.031	1.2±0.231
F2	30.96±0.6	0.156±0.004	0.196±0.002	20±0.043	1.25±0.002
F3	26.56±0.65	0.163±0.009	0.192±0.005	15±0.058	1.10±0.315
F4	27.9±0.7	0.178±0.001	0.212±0.003	16±0.088	1.19±0.615
F5	30.11±0.22	0.166±0.009	0.20±0.009	17±0.174	1.20±0.012
F6	29.2±0.77	0.178±0.003	0.204±0.004	12±0.288	1.14±0.091
F7	21.80±0.54	0.161±0.002	0.178±0.002	9±0.023	1.10±0.002
F8	28.36±0.9	0.192±0.007	0.212±0.006	15±0.068	1.17±0.415

*n=3±SD. SD: Standard deviation, IVH: Ivabradine hydrochloride

Table 5: Results of post-compression characteristics directly compressed tablets of IVH, F1–F8

Formulation code	Percentage weight variation (n=20±SD)	Hardness (kg) (n=3±SD)	Percentage drug content (n=10±SD)	Friability (%) (n=10±SD)	Disintegration time (n=6±SD)	Thickness (mm) (n=3±SD)
F1	1.76±0.25	5.2±0.24	96.59±0.0016	0.55±0.0017	6 min 30 s	3.16±0.045
F2	1±0.05	4.8±0.16	91.4±0.0012	0.99±0.0037	4 min 20 s	3.29±0.037
F3	1.83±1.03	4.2±0.20	93.75±0.0016	0.80±0.0016	7 min 5 s	3.21±0.039
F4	3.25±1.75	5.5±0.20	95.45±0.0012	0.66±0.0024	8 min 55 s	3.41±0.027
F5	2.01±1.09	5.5±0.12	94.88±0.0016	0.62±0.0047	7 min 10 s	3.26±0.035
F6	2.5±0.59	4.8±0.12	93.18±0.0037	0.66±0.0052	6 min 5 s	3.33±0.046
F7	2.16±1.24	4.1±0.16	98.92±0.0016	0.73±0.0054	4 min 50 s	3.12±0.028
F8	2.06±0.99	5.6±0.21	96.5±0.0012	0.72±0.0041	6 min 30 s	3.28±0.042

SD: Standard deviation, IVH: Ivabradine hydrochloride

Table 6: *In vitro* drug release profile of IVH tablets (F1–F4)

Time (h)	Cumulative percentage of drug release			
	F1	F2	F3	F4
0	0	0	0	0
2	1.12±0.02	4.5±0.10	33.75±0.05	21.37±0.09
5	6.75±0.10	19.12±0.09	59.62±0.06	22.5±0.03
8	16.87±0.20	46.12±0.20	81±0.09	30.37±0.02
10	20.25±0.08	72±0.05	90±0.10	50.62±0.07
20	38.25±0.06	84.37±0.07		60.75±0.08
30	43.87±0.05	90±0.08		67.5±0.06
60	48.37±0.09			87.75±0.05
90	87.75±0.05			91±0.10

*n=3±SD. SD: Standard deviation, IVH: Ivabradine hydrochloride

Hausner's ratio from 1.2 to 1.25 suggests free-flowing properties of F1–F8. Hence, all these formulations are compressed as tablets.

Evaluation studies of directly compressed tablets of IVH

Post-compression characteristics of finished tablets of F1–F8 are given in Table 5. As revealed from the values, the percentage weight variation (1–1.75), hardness (4.1–5.6 kg/cm²), drug content (91.4–98.92), friability (0.55%–0.99%), disintegration time (4 min 20 s–8 min 55 s), and thickness (3.12–3.41 mm) are in acceptable limits. The percentage drug content values are also satisfactory.

***In vitro* drug release studies**

The drug release profiles of tablets, F1–F8 and the commercial tablets of IVH are represented in Tables 6 and 7 and in Figs.10 and 11.As

Table 7: *In vitro* drug release profile of IVA tablets F5–F8

Time (min)	Cumulative percentage of drug release				
	F5	F6	F7	F8	Marketed product
0	0	0	0	0	0
2	13.5±0.10	33.75±0.08	41.62±0.09	20.25±0.10	15.55
5	23.62±0.07	41.62±0.05	96.37±0.08	28.12±0.02	99
8	43.87±0.08	51.75±0.02	98.75±0.05	39.37±0.07	
10	50.62±0.05	67.5±0.09		43.87±0.05	
20	66.37±0.07	81±0.10		56.25±0.08	
30	69.75±0.03	90±0.04		77.62±0.08	
60	77.62±0.06			84.37±0.10	
90	84.37±0.07			88.87±0.03	

*n=3±SD. SD: Standard deviation, IVA: Ivabradine hydrochloride

Table 8: Kinetics of drug release of formulations F1–F8

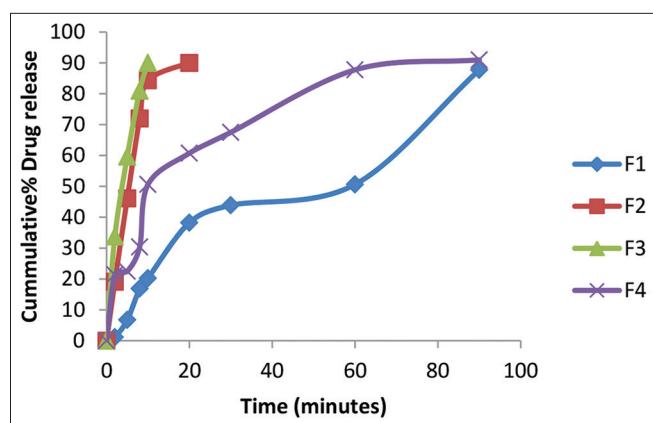| Formulation code	Regression model drug release kinetics		Higuchi (R^2)	Korsmeyer–Peppas	
	Zero-order kinetics (R^2)	First-order kinetics (R^2)		R^2	n
F1	0.856	0.901	0.943	0.925	1.08
F2	0.317	0.902	0.921	0.804	1.88
F3	0.797	0.986	0.993	0.780	2.24
F4	0.402	0.952	0.936	0.727	1.25
F5	0.44	0.848	0.869	0.742	1.26
F6	−0.825	0.955	0.967	0.679	1.64
F7	0.508	0.958	0.951	0.774	2.63
F8	−0.20	0.911	0.930	0.71	1.26

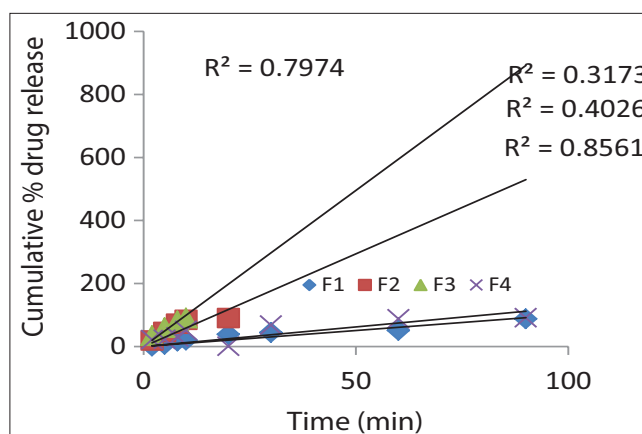Fig. 10: *In vitro* drug release profile of different formulations F1–F4

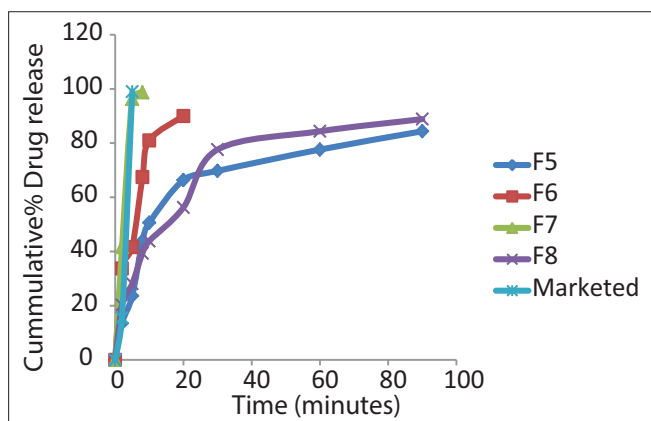Fig. 12: Zero-order kinetics of formulations F1–F4

Fig. 11: *In vitro* drug release profiles ivabradine hydrochloride tablets of formulations F5–F8 and commercial tablet
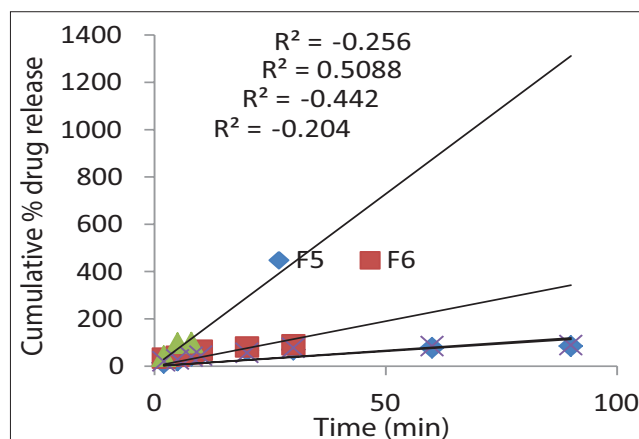

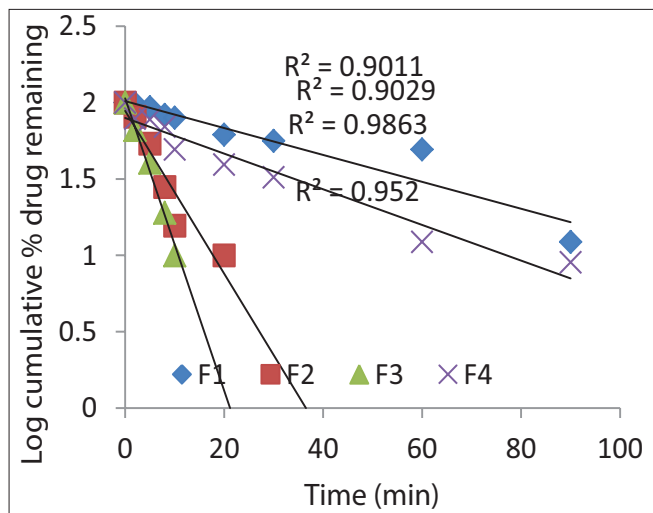Fig. 13: Zero-order kinetics of formulations F5–F8
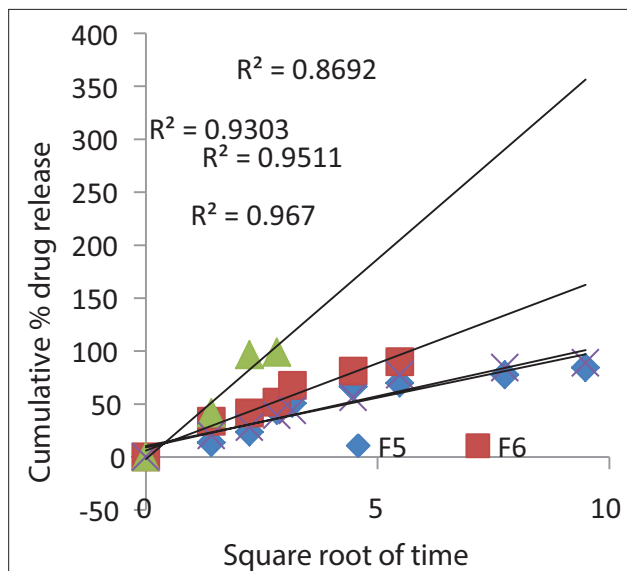
Fig. 14: First-order kinetics of formulations F1–F4
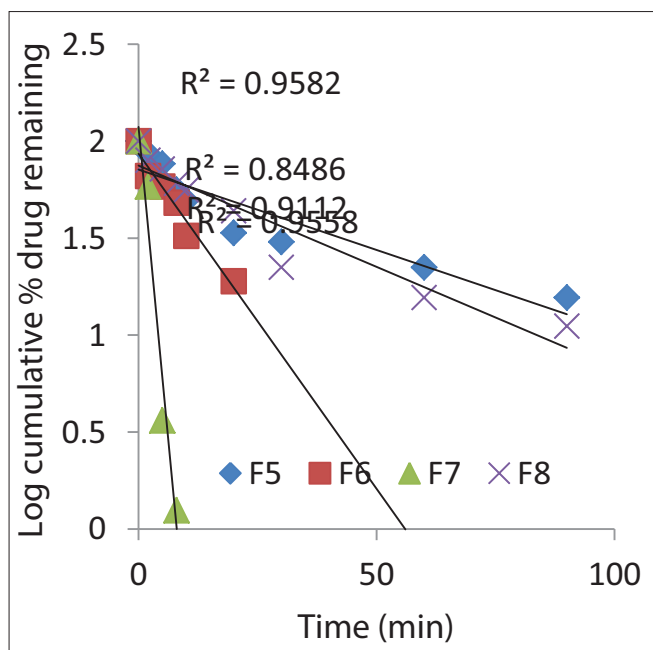

Fig. 17: Higuchi plots of formulations F5–F8

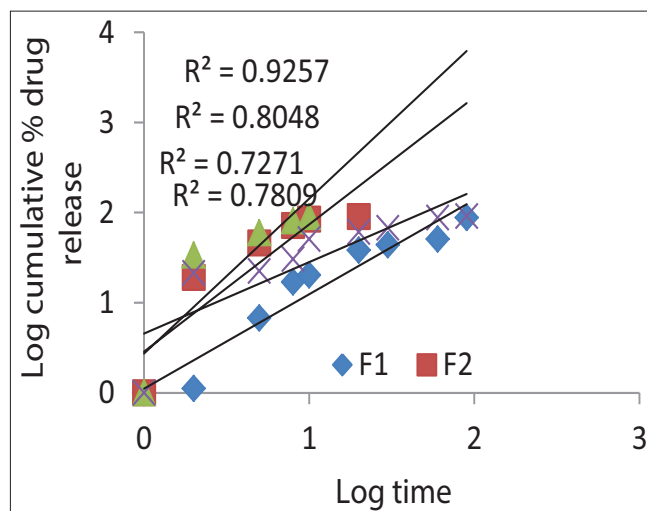**Fig. 15: First-order kinetics of formulations F5–F8**

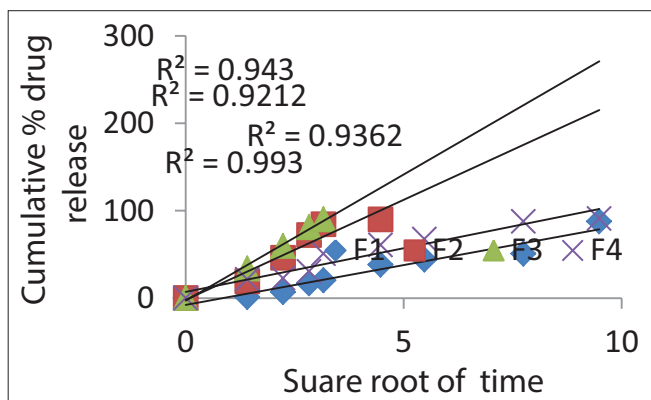**Fig. 18: Korsmeyer–Peppas plots for the formulations F1–F4**

Fig. 16: Higuchi plots of formulations F1–F4
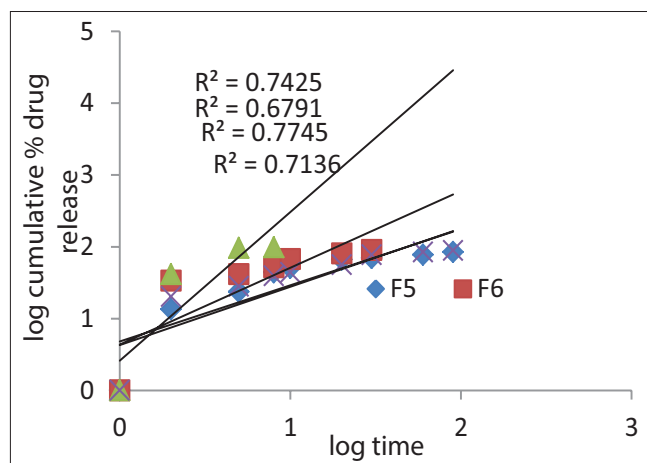

Fig. 19: Korsmeyer–Peppas plots for the formulations F5–F8

these dissolution profiles show fast release from all the formulations prepared using nanocellulose extracted from

our work. Even though disintegration time and hardness values are high like the values of conventional tablets, the dissolution is fast from all tablets. There is no relationship between dissolution and the values of disintegration time and hardness values. This supports the reports related to independent nature of disintegration time on dissolution as per Q6A of ICH as well as hardness [15]. Here, the commercial tablets of IVH have evidenced it as a fast dissolving tablet with drug 99% in 5 min. Even in our work, the tablets made using nanocellulose also exhibited fast release and among all the tablet, F7 showed high release of 96.37% in 5 min and this was considered as a promising formulation.

Kinetics of drug release for all the eight formulations

Various plots of release kinetics directly compressed tablets of IVH are shown in Figs. 12-19 and respective data of correlation coefficient values are given in Table 8.

As per the results, the regression coefficient values (R^2) of all formulations F1–F8 in case of first-order plots are 0.901, 0.902, 0.986, 0.952, 0.955, 0.958, and 0.911. This indicates the drug release following the first-order kinetics. Similarly, it is evident that the mechanism of drug release is diffusion since the Higuchi plots of F1–F8 are having R^2 values 0.943, 0.921, 0.993, 0.936, 0.869, 0.967, 0951, 0.938, and 0.917.

CONCLUSION

From all these, it is concluded that nanocellulose can produce successfully by acid and alkali treatment followed by ball milling and lyophilization and can exploit successfully for design of immediate release tablets of IVH.

Scope

Nanocellulose from plant source will have scope for design of immediate release tablets in case of water-soluble drugs and can have scope for development poorly soluble drugs as conventional release tablet or capsule dosage forms approach for design of fast-release tablets of IVH using nanocellulose similar to the commercially available IVH tablets.

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AUTHORS' CONTRIBUTIONS

Jeevana Jyothi B has designed the plan of present work and responsible for this novel work and preparation of manuscript. Aparna J has done the experiments involved in the research.

CONFLICTS OF INTEREST

The authors have declared no conflicts of interest.

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