Modification & Characterization of Natural Polymer for Development of Dosage Forms

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Abstract: The aim of this work was the chemical modification of pectin by limited acetylation of their free hydroxyl groups to yield high ester pectin and to investigate its swelling and erosion behavior along with the effect on the release pattern of drugs. Propranolol as an antihypertensive drug was formulated as tablet using chemically modified pectin and pure pectin by using wet granulation method and its collision on drug release was studied. Physicochemical characterization of chemically modified pectin, the solubility, gelling or swelling factor was studied. Optimum concentrations of the modified pectin in such a system protect the tablet throughout the gastrointestinal tract. The pectin modified with acetylating agent was found to be promising to modify the release of drugs which are to be delivered throughout GIT. Drug dissolution studies were carried out in buffers of pH 1.2 and 6.8 and the system was designed based on the total GIT transit time concept. The matrix tablet of modified pectin show more release retardant action as compared to pure pectin. Modified dosage form subject to sintering technique it show fast disintegration and dissolution.
Keywords: Pectin, Modified pectin, Controlled release, Propranolol HCl.

Introduction

Drug dosage forms contain many excipients in addition to the active pharmaceutical ingredient(s) to assist in the manufacturing process as well as to optimize drug delivery. They may be natural or synthetic which directly or indirectly influence the extent and/or rate of drug release and absorption. But today, the whole world is increasingly interested in natural drugs and excipients. Natural materials have advantages over synthetic materials because they are non-toxic, less expensive and freely available. Furthermore, they can be modified to obtain tailor made materials for drug delivery systems allowing them to compete with the synthetic products that are commercially available. Polymers have been successfully employed in the formulation of solid, liquid and semi-solid dosage forms and are specifically useful in the design of modified release drug delivery systems. Both natural and synthetic polymers have been investigated extensively for this purpose, but the use of natural polymers for pharmaceutical applications is attractive because they are economical, readily available, non-toxic and capable of chemical modifications, potentially biodegradable and with few exceptions also biocompatible. Thus the use of plant-derived polymers and their semi-synthetic derivatives as excipients in the design of novel dosage forms such as modified release matrix type tablets has increased day-by-day[1]. Pectin, a naturally occurring polysaccharide, in recent years gained increased importance. The benefits of natural pectin are also appreciated by scientists and consumer due to its biodegradability. It is extracted from different sources, e.g. apple, grapes or citrus and is commercially available as a white to light brown powder.
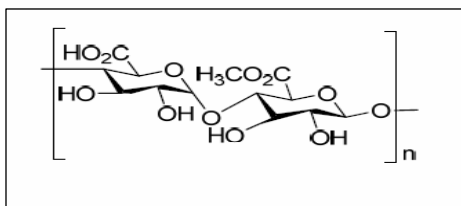
Figure 1: Structure of Pectin

It consists of linear chain of 1-4 linked α-D-galacturonic acid residues with varying degrees of methyl ester substituents. The galacturonic acid polysaccharides are rich in neutral sugars such as rhamnose, arabinose, galactose, xylose and glucose.[2] The pectin can thus associate over a portion of their chains to form acid-pectin gels. Gel forming systems have been investigated widely for sustained drug delivery. Hence recently, pectin has gained increasing research interest in gastroenterological medicine, for use in drug carriers for oral drug delivery [3]. Pectin has high potential as a hydrophilic polymeric material for controlled release matrix drug delivery systems, but its aqueous solubility contributes to undesirable, premature and fast release of the drug from these polysaccharide matrices. One of the options to reduce the high solubility of pectin in aqueous medium is through chemical modification without affecting favorable biodegradability properties[4]. Pectin can be chemically modified by saponification catalyzed by mineral acids, bases, salts of weak acids, enzymes, concentrated ammonium systems and primary aliphatic amines[5].Patients with chronic diseases are increasing day by day. This situation necessitates the use of drugs for a longer period and taking a lot of medicines simultaneously, which may lead to a decrease in patient compliance. This problem is serious for drugs with short biological half- lives because they must be taken more frequently. In this condition controlled release formulation becomes beneficial for reducing dosing frequency and thus increase patient compliance[6].

Material and Method

Material

Propranolol HCL obtained from Lupin Pvt. Ltd. Pune, India. Microcrystalline cellulose, Ployvinylpyrolidone, talc Magnesium stearate purchased from Merck chemicals pvt. Ltd. India.

Method

Modification of Pectin

The pectin was modified by two different techniques as given below.

Method A: Using Acetyl Chloride

A weighed quantity of 10 g pectin was gradually added into the flasks containing 20 ml of freshly prepared 20% v/v, 40% v/v, 60% v/v acetyl chloride in ethanol and stirred for a period of 60 mins in a closed condition over a magnetic stirrer (Table 1). The product was filtered and dried in a hot air oven at 50 C. The dried product was triturated and passed through sieve no 24.[4,5]

Table1: Composition of Modified Pectin

Particulars	MP-20	MP-40	MP-60
Pectin	10gm	10gm	10gm
Acetyl Chloride	04ml	08ml	12ml
Ethanol	16ml	12ml	08ml

Method B: Using Phenyl Acetyl Chloride

Procedure for preparation of Phenyl acetyl halide

1.636 g (0.9772 ml, 0.00136 mol) of redistilled thionyl chloride were placed in a 100 ml two- Necked flask equipped with a dropping funnel and a reflux condenser connected at the top to the gas absorption trap and gently heated on water bath. 1 g of phenyl acetic acid (1.004 ml, 0.01136 mol) was slowly added over a period of 30–40 min. The solid phenyl acetyl chloride was collected.[4,5]

Method B: Using phenyl acetyl chloride

10.0 ml of 20 % w/v phenyl acetyl chloride in ethanol was added gradually to 10 g pectin under stirring over a period of 2 hrs. Reaction product was collected, washed and dried in a hot air oven at 37 ℃.[4, 5]

Selection of Modified Pectin

On the basis of data obtained from the physicochemical characterization of the modified pectin, we have selected product method A for further studies because of its decreased solubility in distilled water but its retaining swelling characters to a desired extent. This chemically modified pectin was used for formulation design to ascertain the release kinetics of ibuprofen from the designed formulation. The release kinetics was in accordance with the anticipations based on the physicochemical characterization of the chemically modified polymer.

Characterization of Modified Pectin

Solubility Studies

The solubility studies of the modified pectin in various solvents like distilled water, chloroform, ethanol were studied. Accurately weighed quantity of 100 mg modified pectin was added to 10 ml of particular solvent in a 50 ml beaker and was shaken for 24 hrs on a water bath shaker. Then the solution was filtered through pre weighed Whatman filtered paper no.41 and the paper was re-weighed after complete drying. The solubility of the modified pectin in a particular solvent was determined by the difference between the final weight and the initial weight of the paper.[4, 5]

Gelling or Swelling factor

A watch glass was taken containing a weighed quantity of 100 mg of modified pectin and to that distilled water was added gradually till no further absorption could be visibly observed[4]. The gelling capacity of the modified pectin was determined by the difference in the weight of watch glass before and after addition and absorption of water.[5]

Determination of Acid value

The acid value is the number which expresses in milligrams the amount of potassium hydroxide necessary to neutralize the free acid present in 1 gram of the 10 g of modified pectin was dissolved in 50 ml of a mixture of equal volumes of ethanol (95%) and ether, previously neutralized with 0.1 M potassium hydroxide to phenolphthalein solution. If the sample does not dissolve in cold solvent, then the flask was connected with reflux condenser and warmed slowly with frequent shaking. 1 ml of phenolphthalein solution was added and titrated with 0.1 M potassium hydroxide until the solution remained faintly pink after shaking for 30 sec. The acid value was calculated from the expression.

$$ACID\ VALUE = 5.61\ n/w$$

Where n is the number of ml of 0.1 M potassium hydroxide required and w is the weight in g of the substance.[4, 5]

Saponification value

The saponification value is the number of milligrams of potassium hydroxide required to neutralize the free acid and to saponify the esters present in 1 g of the sample. In this, 2 g polymer was taken into a 200 ml flask of borosilicate glass fitted with a reflux condenser. 25 ml 0.5 M ethanolic potassium hydroxide solution and a little pumice powder was added and refluxed on a water-bath for 30 mins. 1 ml of phenolphthalein solution was added and titrated immediately with 0.5 M hydrochloric acid (a ml). For the blank, the experiment was repeated in absence of polymer (b ml).The saponification value was calculated from the expression,

$$SAPONIFICATION\ VALUE = 28.05(b-a)/w$$

Where w is the weight of the polymer r(g).

Ester value

Ester value is the amount of the potassium hydroxide (mg) required to saponify the esters present in 1 g of the sample[4, 5]. The ester was calculated from the expression:

ESTER VALUE=Saponification value – acid value

FTIR of Propranolol hydrochloride

The infrared spectrum of Propranolol hydrochloride was recorded using IR- spectrophotometer (Brooker) by the conventional KBr pellet method. The spectrum was scanned over a frequency range 4000-400cm^{-1} with a resolution 4cm^{-1}.

FTIR of Pure Pectin

The infrared spectrum of Pure Pectin was recorded using IR- spectrophotometer (Brooker) by the conventional KBr pellet method. The spectrum was scanned over a frequency range 4000-400cm^{-1} with a resolution 4cm^{-1}.

FTIR of Modified Pectin

The infrared spectrum of Modified Pectin was recorded using IR- spectrophotometer (Brooker) by the conventional KBr pellet method. The spectrum was scanned over a frequency range 4000-400cm^{-1} with a resolution 4cm^{-1}.

Compatibility Studies

Preformulation studies were carried out with potential formulation excipients to determine drug- polymer or excipients interaction/compatibility. Modified polymers and excipients included were Modified Pectin, microcrystalline cellulose as diluents, Ployvinylpyrolidone as disitegrant, magnesium stearate and talc as glidant. Propranolol hydrochloride was uniformly mixed with the excipients and the mixtures were placed in glass vials and vials were closed. Propranolol hydrochloride alone was also placed in similar manner to serve as control. Vials were kept at room temperature. After fifteen days samples were observed for physical change.

Formulation of Pectin Based Propranolol HCl Tablets

Tablet of Propranolol HCl were prepared by using modified pectin MP-20, MP-40, MP-60 at varying ratios using microcrystalline cellulose as diluents, Ployvinylpyrolidone as disitegrant, magnesium stearate and talc as glidant and lubricant respectively. Weighed quantities of Propranolol HCl and modified pectin were triturated and mixed thoroughly[8]. Then MCC, PVP added then triturated in mortar and pestle. The dried granules were lubricated with magnesium stearate, talc in and compressed into flat 6 mm tablets using C-GMP (D TOOLING) 8 Station tablet Compression Machine (CEMACH) press (Table 2).

Table 2: Formulation of Propranolol HCl tablet.

Formulation Code	Quantity mg/tablet			
→	**F1**	**F2**	**F3**	**F4**
Propranolol HCl	**100**	**100**	**100**	**100**
MCC	**125**	**125**	**125**	**125**
Pure Pectin				**100**
MP 20	**100**	**-**	**-**	**-**
MP 40	**-**	**100**	**-**	**-**
MP 60	**-**	**-**	**100**	**-**
PVP	**21**	**21**	**21**	**21**
TALC	**2**	**2**	**2**	**2**
Magnesium Stearate	**2**	**2**	**2**	**2**

Accurately weighed amounts of drug, polymer, and diluents were mixed geometrically in a mortar. This mixture was passed through No.40 sieve and thoroughly mixed in a polythene bag for 15 minutes. The powder

blend was then lubricated with magnesium stearate and talc for 2 minutes and compressed into tablets on a tableting machine using 6-mm round, flat-faced punches. The drug polymer ratio was developed to adjust drug release as per theoretical release profile and to keep total weight of tablet constant for all the fabricated batches under experimental conditions of preparations. The total weight of tablet is 350 mg.[9, 10]

Pre-compression Studies

The powder blend was evaluated for angle of repose, bulk density, tapped density and Carr's index (CI) is an important measure that can be obtained from the bulk and tapped densities.[11, 12, 13]

Post-compression Studies

Drug content

Weigh and powder 20 tablet. Weigh accurately a quantity of the powder equivalent to about 20mg of Propranolol hydrochloride and shake with 20ml of Water for 10 minutes. Add 50ml of methanol to produce 100ml and filter. Dilute 10ml of the filtrate to 50ml With Methanol and measure the absorbance of the resulting solution at the maximum at about 290nm, appendix 5.5. Calculate the content of Propranolol hydrochloride taking 222 as the value of a [1%, 1cm] at the maximum at about 290nm.[14]

Thickness

Twenty tablets from the representative sample were randomly taken and individual tablet thickness was measured by using digital vernier caliper. Average thickness and standard deviation values were calculated.[18]

Hardness

Tablet hardness was measured by using Monsanto hardness tester. From each batch six tablets were measured for the hardness and average of six values was noted along with standard deviations.[18]

Friability Test

From each batch, ten tablets were accurately weighed and placed in the friability test apparatus (Roche friabilator). Apparatus was operated at 25 rpm for 4 minutes and tablets were observed while rotating. The tablets were then taken after 100 rotations, dedusted and reweighed. The friability was calculated as the percentage weight loss.

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

Where W1 = Initial weight of the 20 tablets.W2 = Final weight of the 20 tablets after testing.

Friability values below 0.8% are generally acceptable. [15, 16 17]

Weight Variation Test

To study weight variation individual weights (WI) of 20 tablets from each formulation were noted using electronic balance. Their average weight (WA) was calculated. Percent weight variation was calculated as follows. Average weights of the tablets along with standard deviation values were calculated.

$$\% \text{ weight variation} = (WA-WI) \times 100/ WA$$

As the total tablet weight was 120 mg, according to IP 1996, out of twenty tablets ±7.5 % variation can be allowed for not more than two tablets. According to USP 2004, ±10% weight variation can be allowed for not more than two tablets out of twenty tablets. [15, 16 17]

Disintegration test

Disintegration test was carried out according to Indian Pharmacopoeia for capsules using water as a medium. Six capsules were placed in the disintegration apparatus, and was operated for 30 min.[15, 16 17]

In-Vitro Drug Release Studies

Drug release was assessed by dissolution test under the following conditions: n = 3, USP type II dissolution apparatus (paddle method) at 50 rpm in 900 ml of phosphate buffer pH 7.4 from up to 8 hours, maintained at 37°C ± 0.5°C. An aliquot (5mL) was withdrawn at specific time intervals and replaced with the

same volume of pre-warmed (37°C ± 0.5°C) fresh dissolution medium. The samples withdrawn were filtered through Whatman filter paper No.1 and drug content in each sample was analyzed by UV-visible spectrophotometer at 290 nm.

Stability Studies

Formulated tablets were kept for accelerated stability testing in stability chamber (Thermo lab, Mumbai). Storage conditions were maintained at a temperature of 40°C ± 2°C and relative humidity i.e.75% RH ± 5% RH[107]. The minimum period for testing was selected as per mentioned in ICH guidelines. Within seven days after formulated, tablets were transferred to bottles. The samples designed for accelerated stability study were kept at 40° C and 75% RH in sealed bottles. The samples were withdrawal from stability chamber and tested for 15 days, one month, two month and three months after the date of packaging.

Comparison with marketed product

The promising formulation was compared with marketed product of Propranolol HCl. The evaluation parameters tested and compared were drug content uniformity and *in-vitro* dissolution profile. Drug release was assessed by dissolution test under the following conditions: n = 3, USP type II dissolution apparatus (paddle method) at 50 rpm in 900 ml of phosphate buffer pH 7.4 from up to 8 hours, maintained at 37°C ± 0.5°C. An aliquot (5mL) was withdrawn at specific time intervals and replaced with the same volume of pre-warmed (37°C ± 0.5°C) fresh dissolution medium. The samples withdrawn were filtered through Whatman filter paper No.1 and drug content in each sample was analyzed by UV-visible spectrophotometer at 290 nm.

Results and Discussion

Physical compatibility studies

Drug Excipients compatibility study was done by using FTIR spectroscopy and the physical mixture was also observed. Fourier transform infrared (FTIR) spectral data were taken on a Brooker instrument to find out the chemical stability of the drug with excipients.
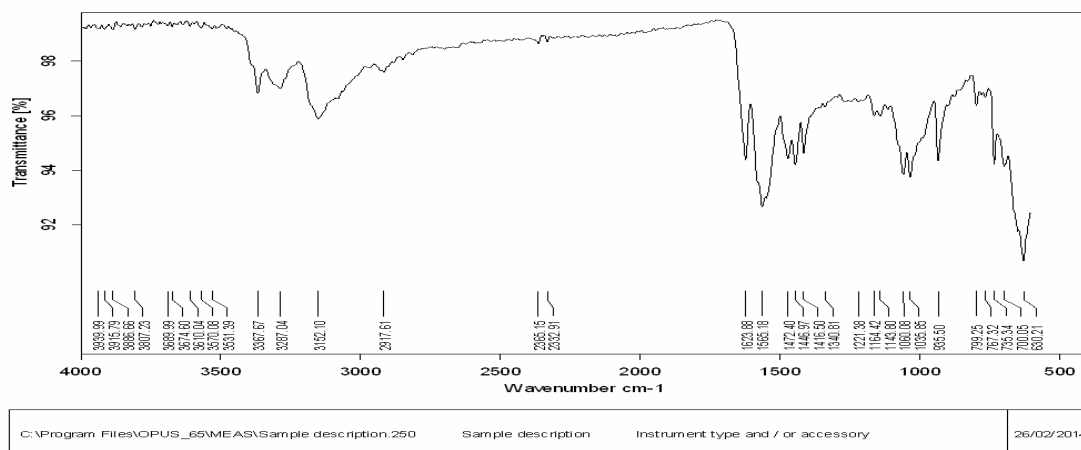

Figure 3: IR-Spectra of Propranolol HCl with excipients

The infra-red absorption spectrum of residue is concordant with the reference spectrum of Propranolol HCL treated in same manner. It may be concluded that, the drug is in the same pure state even in the formulation without interacting with the polymers. After 15 days, samples were observed for physical changes but there were no significant physical changes observed in the formulation of Propranolol HCl along with Modified pectin and excipients used for formulation of tablets (Figure 3). The hydrophilicity of the pectin polymer was reduced by acetylation process with the partial chemical treatment in various concentration of 20%, 40%, and 60%v/v of acetyl chloride in ethanol solution. The obtained modified pectin of different fractions was studied for various physiochemical properties like solubility and swelling property of modified pectin in water decreased with increased degree of acetylation process as compared to pure pectin as depicted in the table no.3 & 4.

Table 3: Solubility parameters

Quantity of polymer (mg)	Solvent	Quantity of modified polymer *d*issolved(mg)		
		MP-20	**MP-40**	**MP-60**
100	Distilled water	48	38	29
100	Chloroform	50	56	59
100	Ethanol	56	63	67

The decreased results of acid value and increased saponification and ester values of modified pectin (MP-20, MP-40, and MP-60) as compared to pure pectin showed that acetylation has occurred with the free hydroxyl groups of the pectin (Table 5).

Table 4: Gelling or swelling factor of modified Pectin

Quantity of polymer	Solvent	Quantity of Water up-take (swelling factor%)			
		Modified Pectin			Pure Pectin(mg)
		MP-20	MP-40	MP-60	
100mg	Distilled Water	0.220gm	0.176gm	0.154gm	0.427gm

Table 5: Physico-chemical parameter between modified pectin and pure pectin

Polymer	Acid value	Saponification value	Ester value
Pure Pectin	19.14	138.23	119.37
Modified Pectin (MP-20)	5.54	227.89	223.41
Modified Pectin (MP-40)	5.37	236.68	231.23
Modified Pectin (MP-60)	4.49	239.43	235.57

Angle of repose of powder was found to be in the range of 22-24^{0}, indicating good flow property and powder blend also evaluated for bulk density, Tapped density and Carr's Index and result was depicted in Table 6. From both these parameters it can be concluded that the powder blend has excellent flow properties.

Table 6: Pre-compression Studies.

Formulation	Angle of repose (%)	Bulk Density(g/ml)	Tapped Density(g/ml)	Carr's Index (%)
F1	25.49	0.215	0.247	14.74
F2	26.27	0.298	0.357	15.38
F3	29.71	0.287	0.315	14.28
F4	28.43	0.285	0.324	15.21

The tablet formulations of Propranolol HCl using various fractions of modified pectin were prepared by direct compression method. The formulations obtained were subjected to unofficial and official tests for tablets and the values obtained within the acceptable range and result was depicted in Table 7.

Table 7: In process quality control of Propranolol HCl tablet.

Formulation Code	Weight variation (mg+_)	Friability Test (%)	Hardness Test(Kg/cm^2)	Drug content (%)
F1	349–+5	0.27	7.2-+0.1	98.87
F2	348-+5	0.31	7.5-+0.2	99.52
F3	351-+5	0.29	7.3-+0.1	98.67
F4	351-+5	0.27	7.2-+0.1	98.87

The results of in-vitro drug release studies showed a sustained release of Propranolol HCl with all the formulations. The dissolution profile of the formulated tablet of Propranolol HCl showed sustained release of

drug at pH 7.4. There is no release of drug more than 30% for first two hours and showed more than 70% release of Propranolol HCl at pH 7.4 after 6hours. It was found that the drug retarding efficiency of modified pectin increased in order of MP-60>MP-40>MP-20 and % cumulative release was depicted in Table 8. The dissolution data obtained were processed by UV Spectrophotometer.

Table 8: In-vitro Release Data. (Higuchi Model)

Best Fit Model-Higuchi Model			
Time	% Cumulative Release		
	F1	F2	F3
0	0	0	0
1	35.45	34.51	33.87
2	39.87	37.87	39.97
3	44.54	47.65	45.65
4	49.98	52.43	54.54
5	58.47358	57.87	58.95
6	72.04697	68.38356	65.87
7	84.69041	82.91507	73.92564
8	92.80626	88.57456	83.65714
	R^2	R^2	R^2
	0.980187	0.978519	0.97455
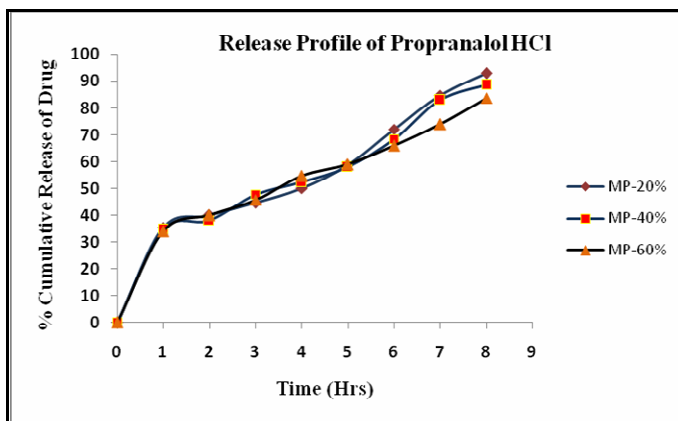
Figure 5: Release Profiles of Propranolol HCl from Modified Pectin

Comparative in-vitro release studies.

The dissolution profile of the marketed tablet of Propranolol HCl and formulated tablet showed sustained release of drug at pH 7.4. There is no release of drug more than 30% for first two hours and showed more than 70% release of Propranolol HCl at pH 7.4 as shown in figure 6.
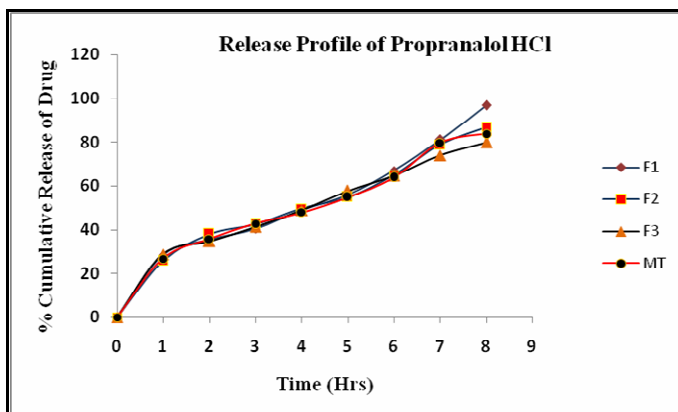

Figure 6: Comparative Release Profiles of Propranolol HCl from Modified Pectin and Marketed tablet (MT).

The IR spectra of all the modified pectin samples remained almost similar but when compared with pure pectin, it was found that the IR spectra of pure pectin having the –OH Stretch of alcohol (3500- 3200cm) shown by strong broad band (Figure 7) were found to be absent in all the IR spectra of modified pectin, confirming the chemical modification of pectin during the acetylation process (Figures 8 -10).
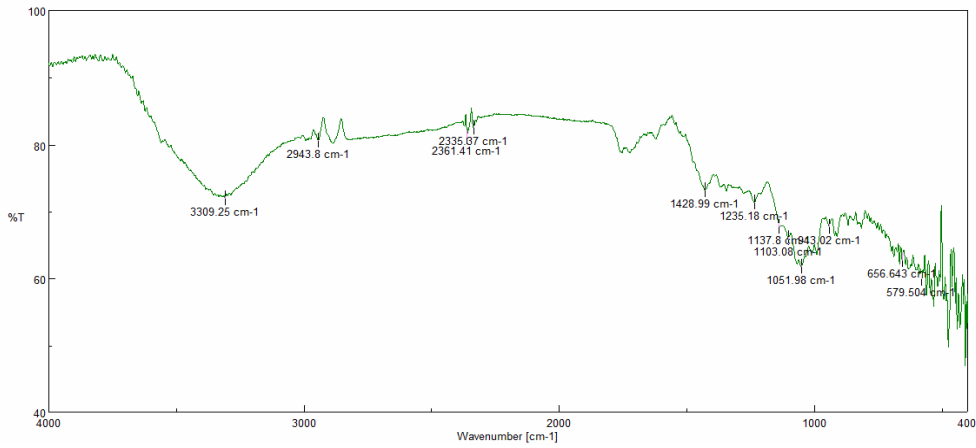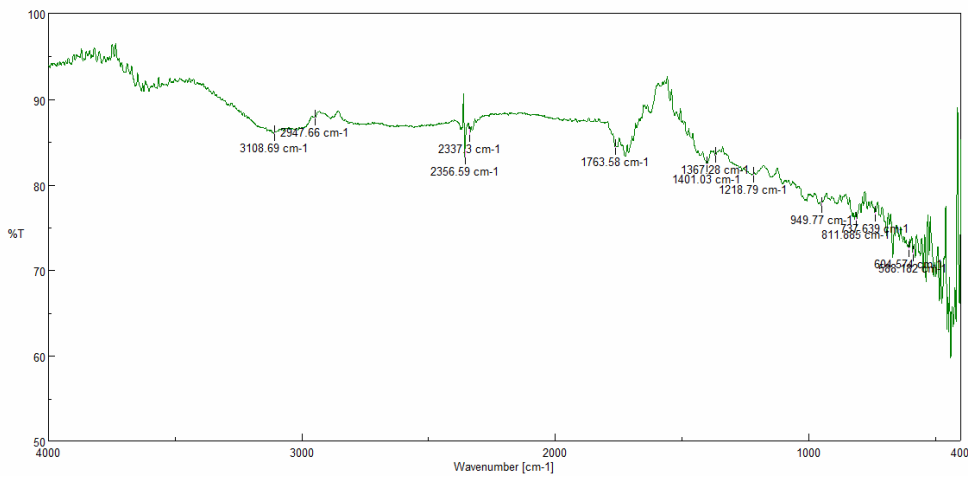

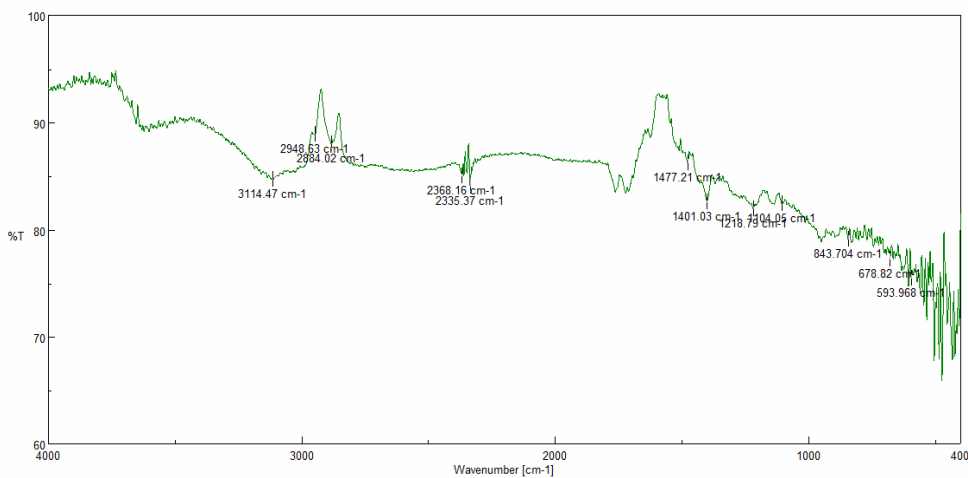**Figure 7: IR Spectra of Pectin**.

Figure 8: IR Spectra of MP-20.
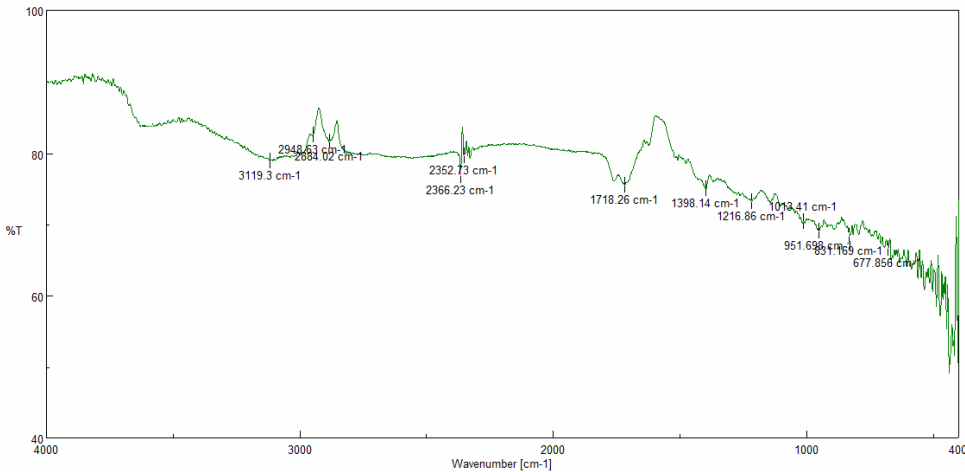

Figure 9: IR Spectra of MP-40.

Figure 10: IR Spectra of MP-60.

Stability Studies

Formulation such as F1, F2 and F3 load during stability studies showed the drug content as shown in Table 9. This indicated that formulation was stable in presence of the excipients used, under accelerated conditions of temperature and humidity.

Table 9: Stability study of Propranolol HCl tablet formulated using Modified Pectin.

Formulation	Drug Content (% w/w) After			
	15 Days	**One month**	**Two month**	**Three Month**
F1	98.23	97.56	97.48	97.13
F2	97.64	97.86	96.31	97.54
F3	97.76	98.45	97.89	98.54

Stability data of an optimized batch load revealed that the percent drug released after 8 hours at 0 day and after 30 and 60 days was same. The dissolution data study indicated that there was no degradation of formulated Propranolol HCl tablet nor was there a change in the release profile. (Figure 11).
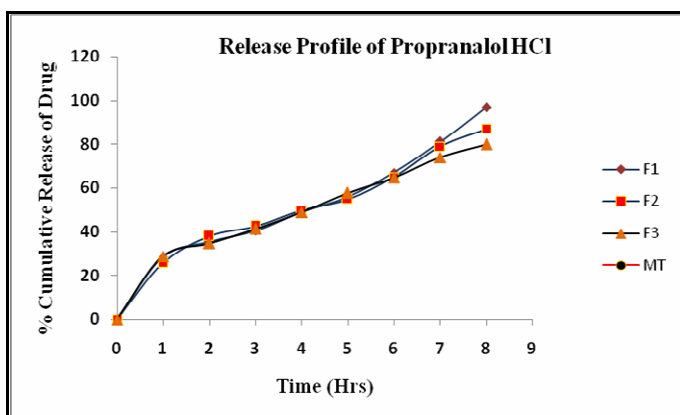

Figure 11: Release Profiles of Propranolol HCl from Modified Pectin

The percent cumulative release was found to be more than 70% at pH 7.4 after 2 hrs. Rate of release of formulated Propranolol hydrochloride tablet using pure pectin was performed using Electro lab dissolution test apparatus with six stage dissolution rate testing apparatus. The dissolution fluid was 900ml of buffer pH 7.4, a speed of 50rpm & a temperature of 37±0.5°C. Since the dissolution process of a tablet depends upon the wetting followed by disintegration of tablet. Release of drug detected in graph that up to 98.02% drug was released after 3 hour (Figure 12).
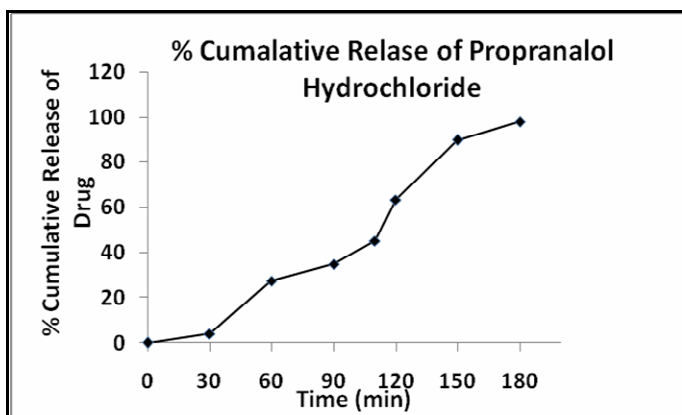
Figure 12: Drug release profile of tablet formulated using Pure Pectin

Conclusion

The pure pectin was chemically modified by acetylation with phenyl acetyl chloride and the obtained modified pectins were characterized for various physico-chemical properties and the results showed the hydrophobicity of the modified pectin. Modified pectin of different fractions was studied for various physiochemical properties like solubility and swelling property of modified pectin in water decreased with increased degree of acetylation process as compared to pure pectin. The decreased results of acid value and increased saponification and ester values of modified pectin (MP-20, MP-40, and MP-60) as compared to pure pectin showed that acetylation has occurred with the free hydroxyl groups of the pectin. The infra-red absorption spectrum of residue is concordant with the reference spectrum of Propranolol HCL treated in same manner. It may be concluded that, the drug is in the same pure state even in the formulation without interacting with the polymers (Figure 3). The IR spectra of all the modified pectin samples remained almost similar but when compared with pure pectin, it was found that the IR spectra of pure pectin having the –OH Stretch of alcohol (3500- 3200cm) shown by strong broad band (Figure 7) were found to be absent in all the IR spectra of modified pectin, confirming the chemical modification of pectin during the acetylation process (Figures 8 - 10).Angle of repose of powder was found to be in the range of 22-24^0, indicating good flow property and powder blend also evaluated for bulk density, Tapped density and Carr's Index and result was depicted in Table 6. From both these parameters it can be concluded that the powder blend has excellent flow properties.

The tablet formulations of Propranolol HCl prepared using modified pectins as a polymer in assorted ratios observed with unofficial and official quality control tests. The results of in-vitro drug release studies showed a sustained release of Propranolol HCl with all the formulations. The dissolution profile of the formulated tablet of Propranolol HCl showed sustained release of drug at pH 7.4. It was found that the drug retarding efficiency of modified pectin increased in order of MP-60>MP-40>MP-20. The *in-vitro* drug release studies are a sign of the drug release retarding competence with the linear increase in the polymer concentration of the formulations. Hence the modified pectin polymer confirmed as drug release retardant in the formulation of oral controlled drug delivery systems (figure 5). Release was slowed in case of both formulations such as marketed tablet and formulated tablet with modified pectin. Similarity factor was calculated by using PCP-Disso-V3and was found to be 78.9. Stability data of an optimized batch load revealed that the percent drug released after 8 hours at 0 day and after 30 and 60 days was same. The dissolution data study indicated that there was no degradation of formulated Propranolol HCl tablet nor was there a change in the release profile. (Figure 11). The percent cumulative release was found to be more than 70% at pH 7.4 after 2 hrs. Rate of release of formulated Propranolol hydrochloride tablet using pure pectin was performed and release of drug detected in graph that up to 98.02% drug was released after 3 hour (Figure 12).

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