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Thermal sintering: a novel technique in the design of gastroretentive floating tablets of propranolol HCl and its evaluation.

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Keywords: gastroretentive, thermal sintering, propranolol HCl, polyethylene oxide.

Abstract. The aim of the present investigation was to formulate thermally sintered floating tablets of propranolol HCl, and to study the effect of sintering conditions on drug release, as well as their *in vitro* buoyancy properties. A hydrophilic polymer, polyethylene oxide, was selected as a sintered polymer to retard the drug release. The formulations were prepared by a direct compression method and were evaluated by *in vitro* dissolution studies. The results showed that sintering temperature and time of exposure greatly influenced the buoyancy, as well as the dissolution properties. As the sintering temperature and time of exposure increased, floating lag time was found to be decreased, total floating time was increased and drug release was retarded. An optimized sintered formulation (sintering temperature 50°C and time of exposure 4 h) was selected, based on their drug retarding properties. The optimized formulation was characterized with FTIR and DSC studies and no interaction was found between the drug and the polymer used.

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Sinterización térmica: Una técnica novedosa en el diseño de tabletas flotantes gastroretentivas de HCl propanolol y su evaluación.

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Palabras clave: gastroretentivo, sinterización térmica, HCl propanolol, óxido de polietileno.

Resumen. El propósito de la presente investigación fue la elaboración de tabletas flotantes de HCL propanolol térmicamente sinterizadas y estudiar los efectos de las condiciones de sinterización sobre la liberación de la droga, así como sobre sus propiedades de flotabilidad *in vitro*. Se seleccionó un polímero hidrofílico, el óxido de polietileno, como polímero sinterizado, para retardar la liberación de la droga. Las fórmulas se prepararon mediante un método de compresión directa y se evaluaron mediante estudios de disolución *in vitro*. Los resultados demostraron que la temperatura de sinterización y el tiempo de exposición tuvieron una gran influencia sobre las propiedades de flotabilidad y de disolución. Se encontró que el intervalo de retardo en la flotación disminuyó, el tiempo total de flotación aumentó y se retardó la liberación de la droga, a medida que aumentaron la temperatura de sinterización y el tiempo de exposición. Se seleccionó una fórmula óptima de sinterización (temperatura de sinterización de 50°C y tiempo de exposición de 4 h), basados en las propiedades retardativas sobre la droga. La fórmula sinterizada se caracterizó mediante estudios FITR y DSC y no se encontró ninguna interacción entre la droga y el polímero utilizado.

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INTRODUCTION

Thermal sintering is a method of heating a polymer in a sintering furnace below its melting point (solid state sintering) until its particles adhere to each other. In this process, polymer particles will undergo fusion or formation of welded bonds between each particle. Sintering is effective when the process reduces the porosity and enhances the mechanical strength of the powder particles (1).

The thermal sintering method involves the exposure of the formulation to a polymer transition temperature in which the polymer forming the matrix slowly softens and welded bonds are formed. The drug particles will be entrapped in the formed matrix, resulting in the controlled release of the active ingredient. However, this method may be applied to only those drugs that are resistant to the temperature of exposure and this may be the limiting factor for many drugs that get degraded at elevated temperatures (2, 3).

Controlled release of oral dosage forms were developed by sintering the polymer matrix by exposing to temperature above the glass transition point of the polymer.

In the present investigation propranolol HCl was selected as a model drug which is a non-selective beta-adrenergic receptor blocking agent used for the treat-

ment of hypertension (4). It is highly lipophilic and almost completely absorbed after oral administration. However, it undergoes high first-pass metabolism and on average, only about 25% of propranolol reaches the systemic circulation (5). Since there were no reports found on the gastroretentive floating drug delivery systems with sintering technology, the present investigation was aimed at developing floating drug delivery systems with thermal sintering technology. Polyethylene oxide (PEO) is a hydrophilic polymer with melting point ranges from 70-80°C, hence in the present investigation it was selected as the polymer of choice for sintering and was proposed to study its applicability on sintering techniques for the design of gastroretentive floating tablets (GRFT) of propranolol HCl.

MATERIAL AND METHODS

Materials

Propranolol HCl was provided by Dr. Reddy's Laboratories Ltd. (Hyderabad, India). PEO (PEO WSR coagulant grade), sodium bicarbonate and magnesium stearate were obtained as gift samples from Unichem Laboratories Ltd (Goa, India). All other reagents and chemicals were of analytical grade.

Apparatus

A 16-station rotary tablet compression machine (Cadmach Machinery Co. Pvt. Ltd.Ahmadabad, India), a dissolution test apparatus (Model: Disso 2000, Labindia Instruments Pvt. Ltd. Mumbai, India), a hot air oven (Shiva Scientific Services, India) and an UV Visible spectrophotometer (Model: SL 210, Elico, India) were used.

Preparation of GRFT of propranolol HCl

All the ingredients sufficient for a batch of 100 tablets according to the formulae mentioned in Table I were passed through the sieve # 40 (425 μm). Drug was geometrically mixed with PEO until a homogeneous blend was achieved. Sodium bicarbonate was added to the above mixture and mixed for 5 min in a polybag. The blend was lubricated with pre-sifted magnesium stearate for 3 min in a polybag. The final blend was compressed into tablets containing 80 mg of propranolol HCl on a 16-station rotary tablet-punching machine using 7mm round plain punches at the compression force of 15-17 KN.

TABLE I
FORMULAE OF THE GRFT OF PROPRANOLOL HCL

Ingredients	PPR 01	PPR 02
Propranolol HCl	80	80
PEO WSR Coagulant	80	60
Sodium bicarbonate	18	16
Magnesium stearate	2	2
Total weight (mg)	180	158

Preparation of thermally sintered floating tablets (TSFT) of propranolol HCl

The formulations were exposed to three different temperatures viz., 40°C, 50°C and 60°C and for four different periods of 1, 2, 3 and 4 h in a hot air oven maintained at the respective temperatures. The tablets were removed after the respective exposure times, cooled to room temperature and stored in a desiccator until further use.

Evaluation of the un-sintered and sintered floating tablets

Tablets were evaluated for physicochemical properties like uniformity of weight, assay, hardness, *in vitro* buoyancy studies and *in vitro* dissolution studies.

In vitro buoyancy studies

All the formulated floating tablets were subjected to *in vitro* buoyancy studies

and 5 tablets were used for each batch (6). The floating lag time was determined in 1 liter glass beaker containing 900 mL of 0.1N HCl. The time required for the tablet to rise to the surface and float was determined as floating lag time. The duration of time the dosage form constantly remained on the surface of medium was determined as the total floating time. Results are mentioned in Table II.

In vitro dissolution studies

In vitro release of propranolol HCl from the prepared floating tablets was studied using an USP XXIV dissolution test apparatus, employing the paddle stirrer (Apparatus-II). 900 mL of 0.1N HCl was used as a dissolution medium maintained at a temperature of 37±0.1°C and the paddle was rotated at 50 rpm (7). Samples of 5 mL were withdrawn and immediately replaced with 5 mL of fresh medium maintained at 37±0.1°C. The filtered samples were suitably diluted with the dissolution medium wherever necessary and the absorbance of the samples was measured at 289 nm. The dissolution experiments were done in triplicate.

Release kinetics

Kinetic models describe the release profile as a function of some parameters related to the pharmaceutical formulations with the help of mathematical equations for easy quantitative interpretation of the values. These methods seem to be useful in the formulation development stage which includes zero order (8), first order (9), Higuchi (10), Korsmeyer-Peppas (11) and Hixson-Crowell (12) models. The model with the highest correlation coefficient (r) was judged to be a more appropriate model for the dissolution data.

Model	Equation
Zero-order	$Q_t = Q_0 + K_0 t$
First-order	$\log C = \log C_0 - K_1 t/2.303$
Higuchi	$Q = K_H t^{1/2}$
Hixon-Crowell	$\left(W_0^{1/3} - W_t^{1/3}\right) = Kt$
Korsmeyer-Peppas	$M_t/M_\infty = K_K . t^n$

Q_t: amount of drug released in time t, Q_0: initial amount of drug in the tablet, C_0: Initial concentration of drug, Q: active fraction released per unit of surface, W_0: initial amount of drug in the pharmaceutical dosage form, W_t: remaining amount of drug in the pharmaceutical dosage form at time t, M_t: The amount of drug released at time t and M_∞: Amount released at time ∝, thus the $M_t \backslash M_\infty$: Fraction of drug released at time t, K_o, K_1, K_H, K, K_K - Rate order constants.

According to the Korsmeyer-Peppas equation, the release exponent 'n'value is used to characterize different release mechanisms. If the n value is 0.5, the release mechanism follows a Fickian diffusion. If n value is $0.45 < n < 0.89$ (for cylindrical), the mechanism follows a non-Fickian (anomalous) diffusion and when n=0.89 it will be a non-Fickian case II transport and if n>0.89 it will be a non-Fickian super case II transport (11).

X- ray powder diffractometry (XRPD)

XRPD studies of pure drug, polymer and for optimized formulation were performed with a RIGAKU 30 KvX-ray diffractometer (D/MAX-B, Japan) using Ni filtered Cu-K(α) radiation, a voltage of 35 kV, a current of 20 mA and receiving slit of 0.2 inches. The sample was analyzed over 2θ range of 2-45° with scan step size of 0.020° and scan step time of 1 sec.

Crystal size was calculated by the following formula (13, 14):

TABLE II
TABLETTING AND BUOYANCY CHARACTERISTICS OF UN-SINTERED AND SINTERED PROPRANOLOL HCL FLOATING TABLETS

Sintering temperature & time	Weight[x] (mg)	Assay[y] (%)	Hardness* (Kg/cm^2)	Friability** (%)	Floating lag time[z] (sec)	Total Floating time[z] (h)
PPR 01						
Unsintered	180± 0.98	100.11±1.2	4-6	0.29	145±5	7±1
40°C- 1 h	179±1.66	98.12± 1.34	4-6	0.31	141±4	7±1
40°C- 2 h	180±1.11	100.12±1.28	4-6	0.12	147±8	7±1
40°C- 3 h	178±1.02	100.67±1.12	4-6	0.45	140±4	7±1
40°C- 4 h	179±1.19	100.96±1.21	4-6	0.35	139±6	7±1
50°C- 1 h	181±1.54	100.12±1.43	4-6	0.39	130±4	9±1
50°C- 2 h	182±1.68	99.65±1.94	4-6	0.46	115±5	10±1
50°C- 3 h	181±1.43	99.72±1.28	4-6	0.41	101±7	12±1
50°C- 4 h	180±1.29	100.12±0.30	4-6	0.39	99±2	13±1
60°C- 1 h	181±1.12	100.35±0.51	4-6	0.38	103±4	12±1
60°C- 2 h	179±1.20	100.45±1.07	4-6	0.37	99±2	13±1
60°C- 3 h	178±1.21	100.02±0.99	4-6	0.41	87±1	14±1
60°C- 4 h	182±1.72	99.55±1.21	4-6	0.44	81±7	15±1
PPR 02						
Unsintered	158±1.51	99.12±0.9	4-6	0.30	167±5	8±1
40°C- 1 h	157±1.37	99.99±0.34	4-6	0.16	164±9	8±1
40°C- 2 h	159±1.09	99.92±1.42	4-6	0.21	166±7	8±1
40°C- 3 h	160±1.21	99.92±0.99	4-6	0.33	161±4	8±1
40°C- 4 h	158±1.72	98.55±1.21	4-6	0.16	159±3	8±1
50°C- 1 h	156±1.36	99.43±1.11	4-6	0.48	142±5	9±1
50°C- 2 h	157±1.45	99. 85±0.22	4-6	0.35	121±7	10±1
50°C- 3 h	157±1.66	100.11±1.29	4-6	0.31	111±10	11±1
50°C- 4 h	158±1.11	99.12±1.40	4-6	0.12	103±6	12±1
60°C- 1 h	157±1.02	98.99±1.01	4-6	0.45	110±12	10±1
60°C- 2 h	159±1.19	98.92±1.21	4-6	0.35	101±14	11±1
60°C- 3 h	158±1.54	99.92±0.99	4-6	0.39	92±10	12±1
60°C- 4 h	160±1.17	98.55±1.21	4-6	0.44	87±8	13±1

x: mean±s.d. (n=20); y: mean ± s.d. (n=10); * n=5;** n= 20; z: mean±s.d. (n=5).

$$D = \frac{k\lambda}{\beta \cos\theta} \quad [1]$$

where k= Scherer's constant (0.89), λ = X-ray wavelength (0.1549 nm), β = Peak width at half of its height or FWHM (Full width at half max) and θ = Bragg angle.

Fourier transformation-infrared spectroscopy (FTIR)

Fourier transform infrared spectroscopy (FTIR) was used to identify drug-excipient interaction. Samples were analyzed by the potassium bromide pellet method in an IR spectrophotometer (Shimadzu, Japan, FTIR 8700) in the region between 3500-500 cm^{-1}.

Differential scanning calorimetry (DSC)

Differential Scanning Calorimetric analysis of drug, polymer and optimized formulation were done using a Differential Scanning Calorimeter (Mettler Toledo StarSW 8.10, Switzerland, Model: DSC 822). Samples of 8-10 mg of were weighed in an aluminum pan and were heated under nitrogen atmosphere from 5°C to 250°C.

RESULTS AND DISCUSSION

All the un-sintered (initial tablets) as well as thermally sintered formulations of propranolol HCl prepared using PEO, complied with compendia standard for uniformity of weight. The hardness for all the formulations was found to be in the range of 4-6 kg/cm^2. The drug content estimated was found to be in the range of 98% to 101%. The percentage weight loss in the friability test was found to be less than 0.5%.

Thus all the formulations were found to be of good quality fulfilling all the official requirements.

Floating lag times of all the formulations were within the range of 81 to 167sec (Table II). As the sintering temperature increased the floating lag time was found to be decreased, may be due to decreasing porosity. During the sintering process, the void spaces between the particles might decrease and each particle will exposed to the surface of the gastric fluid quickly, which leads to a decrease in the floating lag time. Total floating times of all the formulations were in the range of 7-15 h. As the sintering temperature increased the total floating time was increased, may be due to the formation of strong welded bonds between the particles, which makes tablet intact for a longer period. Sintering time was inversely proportional to floating lag time and directly proportional to total floating time.

The cumulative percent drug released from sintered and non sintered formulations are shown in the Figs. 1-6. From the results, it was observed that there was no change in the dissolution profile of the formulation when it was exposed to 40°C, which was a positive symptom for stability studies, indicating that the formulation may not effect at accelerated stability conditions (40°C & 75% RH). The formulation of PPR 01 when exposed to 50°C for 1, 2, 3 and 4 h released more than 95% of the drug in 10, 10, 12 and 13 h respectively. Formulation PPR 01 when exposed to 60°C for 1, 2, 3 and 4 h retarded the drug for up to 12, 13, 14 and 15 h respectively. The formulation PPR 02 (without sintering conditions) retarded the drug up to 8 h only and tablets of the same batch at 50°C for 1, 2, 3 and 4 h retarded the drug up to 8, 10, 11 and 12 h respectively and at 60°C for 1, 2, 3 and 4 h retarded the drug up to 10, 11, 12 and 13 h respectively.

From the results, it was observed that as the concentration of polymer increases at constant sodium bicarbonate concentration, release of the drug was retarded which may be due to increased intensity of air pockets surrounding the gellified surface of the tablet (15).

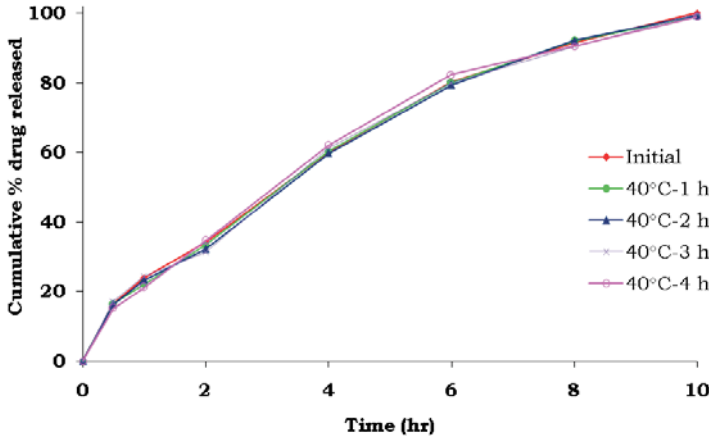

Fig. 1. Dissolution profile of un-sintered and sintered floating formulations of PPR 01 exposed to 40°C.

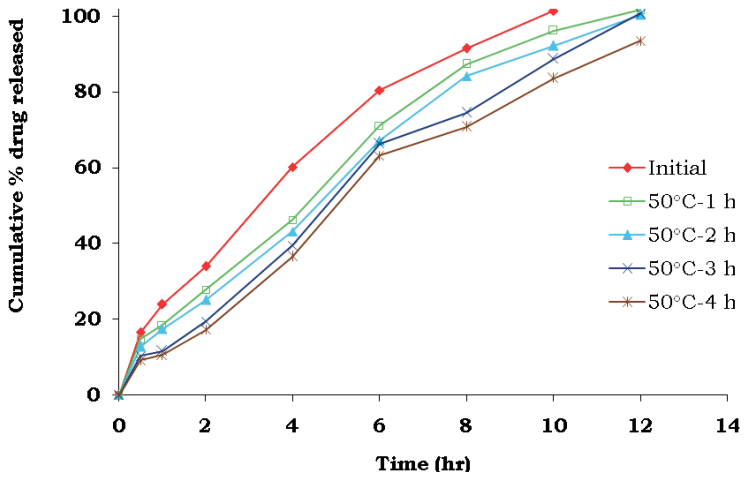

Fig. 2. Dissolution profile of un-sintered and sintered floating formulations of PPR 01 exposed to 50°C.

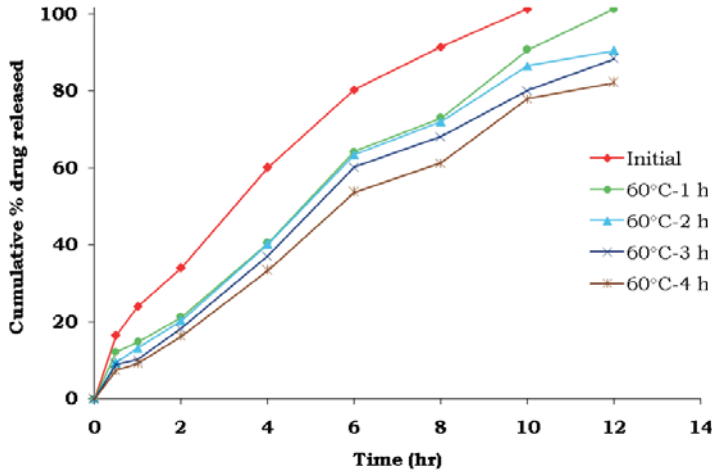

Fig. 3. Dissolution profile of un-sintered and sintered floating formulations of PPR 01 exposed to 60°C.

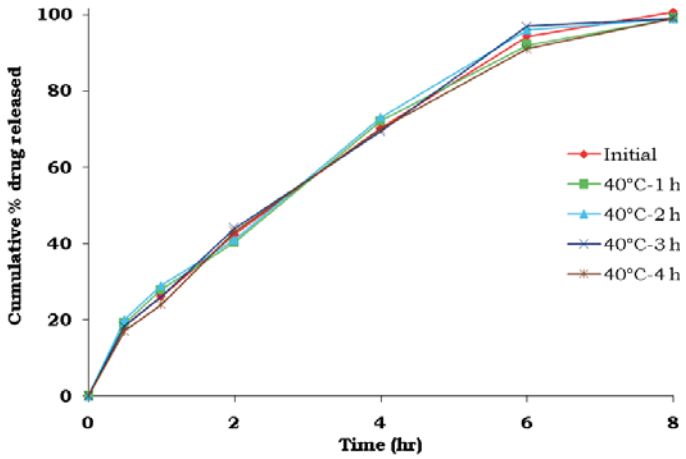

Fig. 4. Dissolution profile of un-sintered and sintered floating formulations of PPR 02 exposed to 40°C.

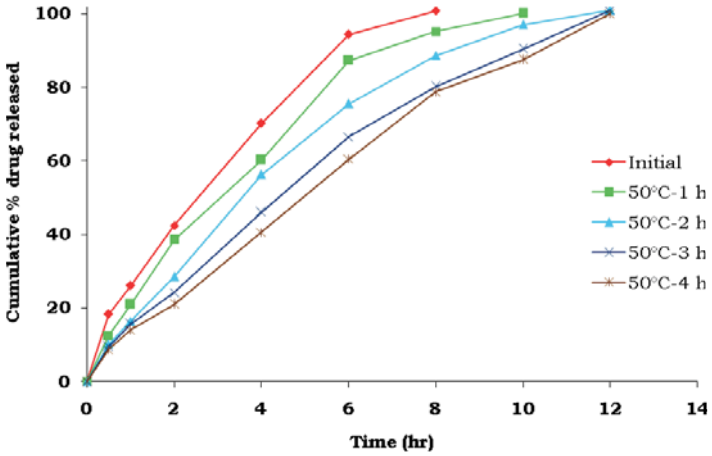

Fig. 5. Dissolution profile of un-sintered and sintered floating formulations of PPR 02 exposed to 50°C.

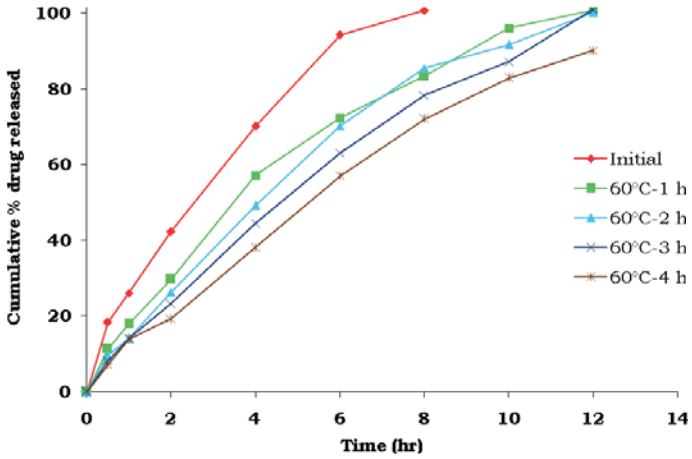

Fig. 6. Dissolution profile of un-sintered and sintered floating formulations of PPR 02 exposed to 60°C.

As the sintering temperature and sintering time increases, release of the drug was decreased. The drug retarding property might be due to the formation of the welded bonds by softening of the polymer to which the drug particles might have been entrapped in the matrix formed which results in the controlled release of drug.

Results of fitting the dissolution profiles to the various kinetic models are given in Table III. Release from un-sintered formulations PPR 01 & PPR 02 followed first order kinetics with a non-Fickian diffusion mechanism. Sintered formulations of PPR 01 followed first order kinetics with a non-Fickian diffusion mechanism until the sintering temperature of 40°C for 4 h. On further increments of sintering temperature and time it followed zero order kinetics with erosion mechanism. Whereas sintered formulations of PPR 02 followed first order kinetics with a non-Fickian diffusion mechanism until the sintering temperature and time reaches 50°C and 2 h respectively.

When the sintering time increases to 3-4 h, it followed zero order rate kinetics with non-Fickian diffusion mechanism. For further increment of sintering temperature and time, the formulations followed zero order kinetics with erosion mechanism.

From the *in vitro* dissolution data and also due to the low proportion of the polymer compared to PPR 01, the formulation PPR 02 obtained at sintering temperature 50°C for 4 h was selected as an optimized formulation. Optimized formulation followed first order rate kinetics with non-Fickian diffusion mechanism.

X- ray Powder Diffractometry (XRPD)

The X-ray diffractograms of propranolol HCl (Fig. 7) showed sharp peaks at 8.401, 9.742, 12.521, 12.860, 16.759, 17.199, 18.678, 19.339, 19.539, 19.918, 21.241, 22.119, 22.460, 23.697, 25.062, 25.439, 25.839, 26.418, 27.081, 29.580, 33.639 and 34.941 angle (°2 θ) having the crystalline size of 29.88, 33.63, 34.83, 41.77, 36.99, 45.86, 63.58, 19.02, 17.00, 46.55, 49.07, 22.73, 27.35, 43.28, 46.71, 37.03, 30.90, 58.70, 39.19, 26.55, 36.02, 32.88 and 44.57 nm respectively indicating the crystallinity of the drug. The average crystalline size of the pure drug was 37.57 nm.

Pure polymer PEO (Fig. 8) showed sharp peaks at 14.679, 15.120, 18.392, 18.680, 19.160, 22.041, 23.022, 23.320, 23.539, 24.160, 26.221, 26.939, 27.940, 36.318 and 39.719 angle (°2 θ) indicating its crystallinity having the size of 19.89, 23.00, 61.25, 15.35, 27.74, 29.93, 14.91, 11.90, 27.94, 23.70, 34.41, 28.22, 39.99, 29.17 and 28.34 nm respectively. The average crystal size was found to be 27.72 nm.

The thermally sintered optimized formulation showed characteristic peaks of pure drug and PEO with minor shift and less intensity at 12.598, 16.801, 17.279, 18.520, 18.720, 19.279, 21.318, 22.179, 22.420, 23.180, 23.380, 23.618, 25.179, 25.480, 26.380, 27.082, 29.119, 29.301, 30.439, 34.659, 39.181 and 44.661 angle (°2 θ) having the size of 27.32, 26.83, 32.44, 31.85, 32.39, 22.73, 17.82, 36.60, 18.17, 11.54, 10.77, 9.85, 9.00, 34.61, 14.57, 45.83, 33.39, 27.54, 14.77, 25.58, 71.06, 30.97, 42.80 and 50.39 nm respectively. It showed disappearance of peaks at 8.401, 9.742, 18.678, 26.418, 29.580, 33.639 and 34.941 angle (°2 θ) (Fig. 7). From the results, it was observed that the crystallinity of the drug was decreased by the addition of PEO, may be due to the fine dispersion of the drug in the softening polymer at its transition temperature. The average crystal size of the optimized formulation was found to be 28.45 nm.

TABLE III
CORRELATION COEFFICIENT VALUES AND RELEASE KINETICS OF UN-SINTERED AND SINTERED PROPRANOLOL HCL FLOATING TABLETS

Sintering temperature & time	Zero order		First order		Higuchi	Erosion	Peppas	
	Ko	r	Ki	r	r	r	n	r
PPR 01								
Unsintered	9.82	0.9782	0.2948	0.9897	0.9980	0.9933	0.6555	0.9955
40°C- 1 h	9.85	0.9776	0.3012	0.9878	0.9947	0.9919	0.6853	0.9954
40°C- 2 h	9.84	0.9791	0.2999	0.9851	0.9923	0.9917	0.6718	0.9937
40°C- 3 h	9.77	0.9771	0.2833	0.9924	0.9835	0.9914	0.6605	0.9892
40°C- 4 h	9.81	0.9732	0.2934	0.9950	0.9951	0.9914	0.6946	0.9938
50°C- 1 h	8.59	0.9830	0.2971	0.9671	0.9872	0.9898	0.7354	0.9954
50°C- 2 h	8.45	0.9870	0.2430	0.9806	0.9852	0.9924	0.7514	0.9948
50°C- 3 h	8.48	0.9919	0.2047	0.9805	0.9778	0.9916	0.7016	0.9958
50°C- 4 h	7.99	0.9899	0.2070	0.9746	0.9815	0.9924	0.7007	0.9948
60°C- 1 h	8.37	0.9938	0.2114	0.9652	0.9800	0.9868	0.7168	0.9952
60°C- 2 h	7.84	0.9866	0.1962	0.9813	0.9866	0.9964	0.708	0.9941
60°C- 3 h	7.56	0.9941	0.1720	0.9904	0.9841	0.9879	0.7846	0.9951
60°C- 4 h	7.15	0.9918	0.1884	0.9376	0.9805	0.9847	0.7096	0.9967
PPR 02								
Unsintered	12.5	0.9766	0.4468	0.9869	0.9913	0.9902	0.6924	0.9962
40°C- 1 h	10.8	0.9612	0.3245	0.9845	0.9956	0.9910	0.6812	0.9454
40°C- 2 h	10.4	0.9791	0.2999	0.9851	0.9943	0.9871	0.6718	0.9387
40°C- 3 h	10.7	0.9771	0.2833	0.9924	0.9974	0.9835	0.6605	0.9457
40°C- 4 h	9.81	0.9732	0.2934	0.9950	0.9949	0.9845	0.6946	0.9142
50°C- 1 h	10.2	0.9697	0.3696	0.9837	0.9956	0.9888	0.6833	0.9916
50°C- 2 h	8.76	0.9722	0.3233	0.9754	0.9977	0.9895	0.7828	0.9914
50°C- 3 h	8.47	0.9892	0.2226	0.9876	0.9982	0.9875	0.7942	0.9971
50°C- 4 h	8.40	0.9939	0.2013	0.9856	0.9813	0.9516	0.7932	0.9966
60°C- 1 h	8.34	0.9924	0.2881	0.9678	0.9922	0.9942	0.7149	0.9936
60°C- 2 h	8.31	0.9928	0.2503	0.9907	0.9875	0.9981	0.7074	0.9949
60°C- 3 h	7.75	0.9952	0.2006	0.9918	0.9858	0.9987	0.7106	0.9984
60°C- 4 h	7.24	0.9943	0.1863	0.9883	0.9862	0.9876	0.7935	0.9949

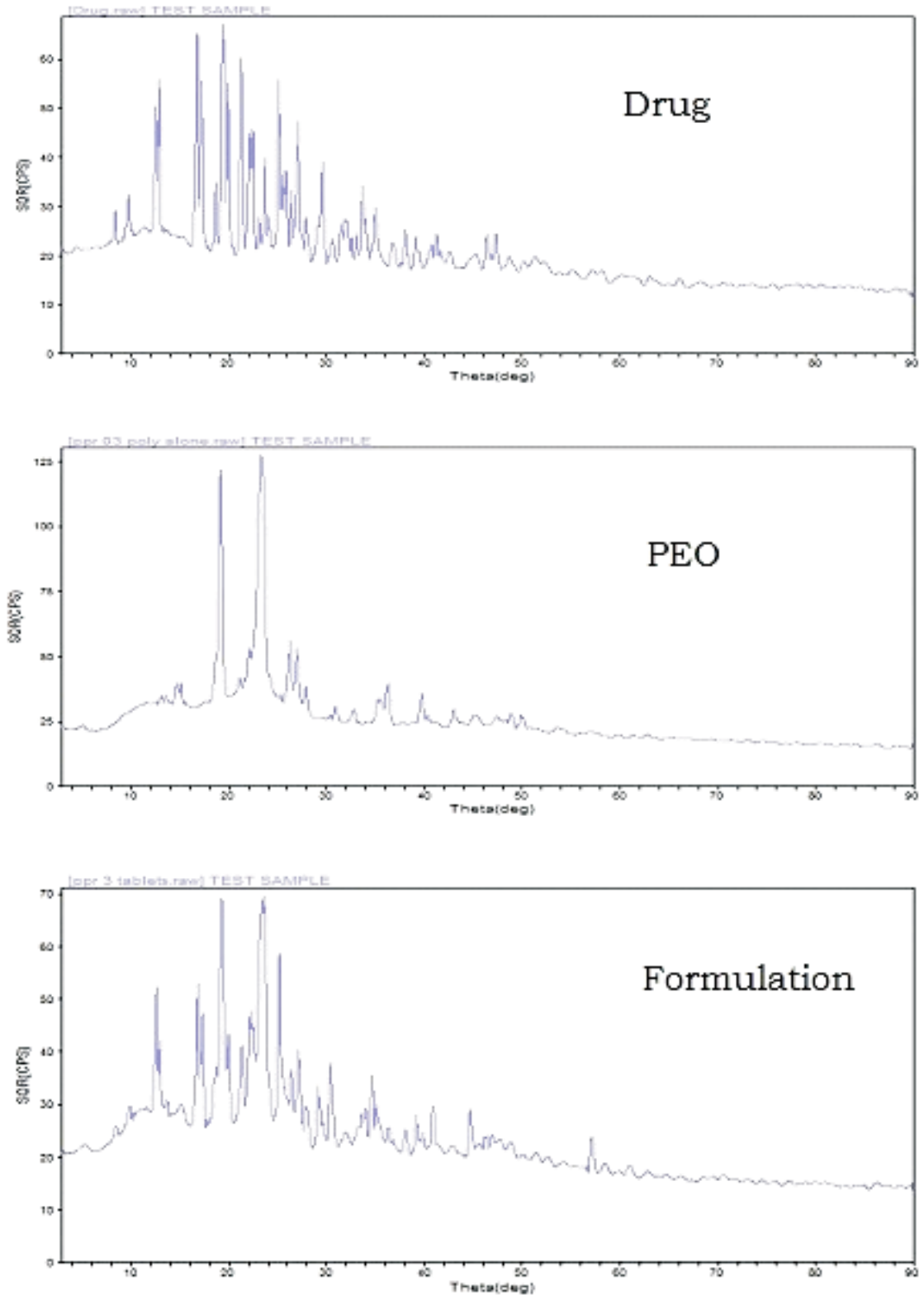

Fig. 7. PXRD patterns of propranolol HCl, PEO and thermally sintered optimized formulation.

Fourier transformation infrared spectroscopy

The FTIR spectrum of propranolol HCl, PEO and Optimized formulation were showed in Fig. 8. Propranolol HCl showed characteristic secondary amine –N–H stretch at 3280cm^{-1}, C-H stretch at 2964 cm$^{-1,}$ aryl C=C stretch at 1579 cm$^{-1,}$ aryl -CH_2 asymmetric stretch at 1240 cm$^{-1,}$ aryl -CH_2 symmetric stretch at 1030 cm^{-1} and the peak at 798 cm^{-1} due to alpha- substituted naphathalene (16).

The FTIR spectrum of PEO showed the characteristic alcoholic –OH stretch at 3433 cm^{-1}, -C-O-C asymmetric stretch at 1260 cm^{-1} and -C-O-C symmetric stretch at 1060 cm^{-1}.

Thermally sintered optimized PEO based formulation showed all the characteristic peaks of propranolol HCl with minor shifts. This spectrum showed secondary amine –N–H stretch at 3280cm^{-1}, C-H stretch at 2963 cm$^{-1,}$ aryl C=C stretch at 1577 cm$^{-1,}$ aryl -CH_2 asymmetric stretch at 1241 cm$^{-1,}$ aryl -CH_2 symmetric stretch at 1031cm^{-1} and the peak at 797 cm^{-1} due to alpha-substituted naphthalene.

Differential scanning calorimetry

The DSC thermogram of propranolol HCl, PEO and optimized formulation are shown in the Fig. 9. The DSC thermogram of pure drug propranolol HCl showed a sharp endothermic melting peak at 165.12°C, similarly PEO at 73°C that corresponds with the respective melting points. The optimized formulation showed sharp endothermic peaks at 71.2°C and 159.37°C, representing polymer and drug peaks respectively, which indicated that decrease in the energy change of melting endotherm, which may be due to the intimate mixing of drug with polymer (17).

The changes observed in the X-ray Diffractograms, DSC and absence of any changes in the FTIR spectra for the selected formulations indicated that there was no chemical interaction between drug and PEO when exposed to thermal sintering.

CONCLUSION

The concept of thermal sintering was studied in order to reduce the polymer

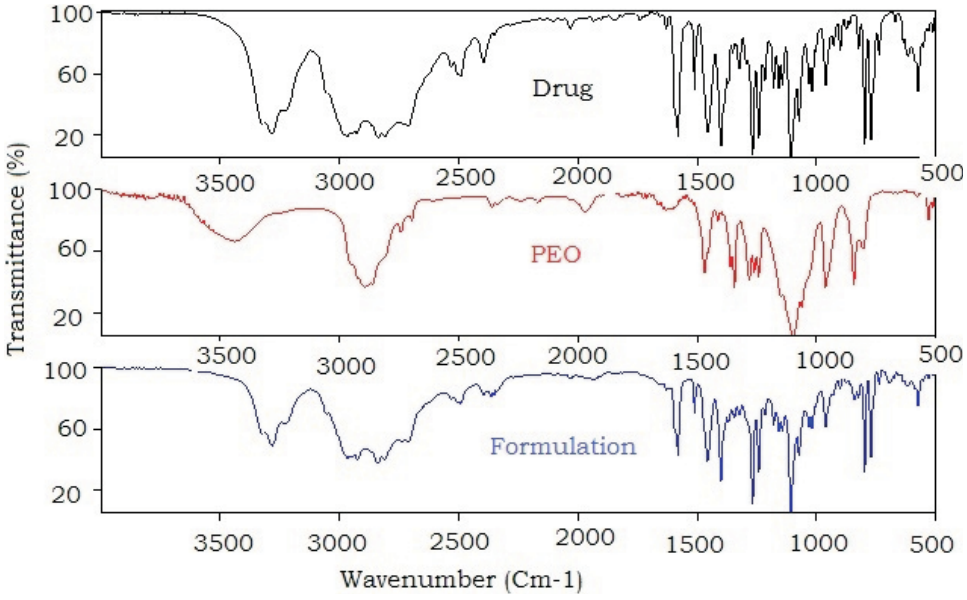

Fig. 8. FTIR spectra of propranolol HCl, PEO and thermally sintered optimized formulation.

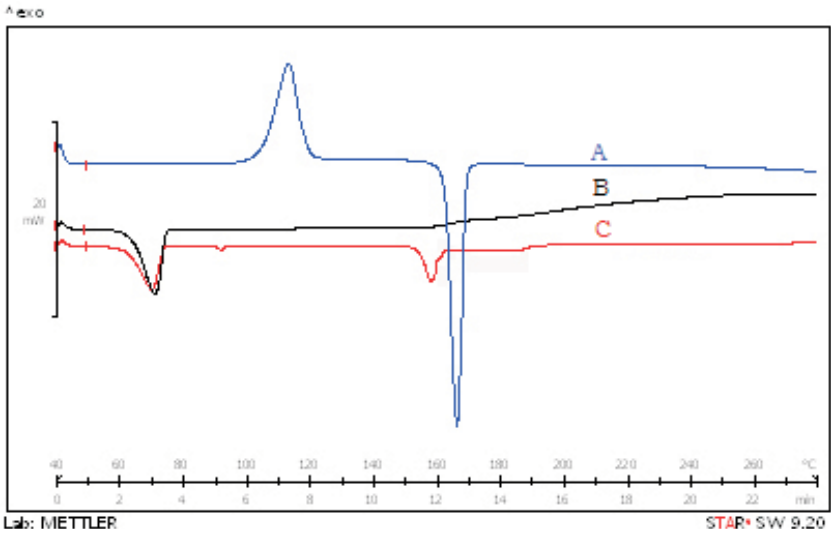

Fig. 9. DSC thermogram of A) propranolol HCl, B) PEO, C) optimized formulation.

quantity with the desired dissolution profile. From the experimental data, it is concluded that floating lag times were decreased and total floating times were increased with duration of exposure of sintering temperature. In addition *in vitro* drug release was retarded with the increase in the duration of exposure to sintering temperature. Hence it can be concluded that the thermal sintering technique can be used in the design of GRFT of propranolol HCl using PEO as a retarding polymer.

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