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Design of sustained release pellets of aceclofenac using cow ghee as hot melt coating agent

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Abstract: The objective of the present study was to design aceclofenac sustained release pellets using cow ghee (CG) as an important hot melt coating (HMC) agent. The pellets were coated by HMC technique using Cg and ethyl cellulose composition by using conventional coating pan without the use of spray system. The prepared aceclofenac pellets were characterized for drug content and physico-chemical properties. Stability studies were performed for a period of 6 months at $40^0 \pm 2^0$ C and 75± 5% relative humidity. Prepared aceclofenac pellets showed good surface morphology and smooth texture which was confirmed by scanning electron photomicrograph. HMC technique is easy rapid and simple method with no agglomeration seen during coating. In vitro release from pellets at a given level of coating and for present pellets size was dependent upon the physico-chemical properties of the drug. Release kinetics indicates approximately zero order release pattern. HMC pellets were stable during the course of stability study. Aceclofenac pellets using CG with ethyl cellulose by HMC technique was successfully prepared.
Key words: pellets; sustained release dosage form; hot melt coating.

Introduction

The advantages of multiple-unit dosage forms over the single-unit ones have been demonstrated by several investigators.[1–4] Coating is a vital stage in the formulation of pharmaceutical dosage form where ultimate objective is to modify drug release or to achieve superior aesthetic value. Coating enhances the physical and chemical protection. The multiunit controlled release dosage forms are usually manufactured by coating the drug-loaded pellets or granules with gastrointestinal fluid-insoluble polymers. The coating of particulates such as powders, granules, pellets and tablets to produce controlled release dosage form is becoming increasingly popular, mainly due to the advances in fluidized-bed process as well as availability of new coating materials.[5]

Film-coating processes often require solvent, i.e., water, organic solvents or mixture. The use of organic solvents may lead to environmental problems, solvent residues and excessive costs of recovery. The aqueous solvent generally prolongs the duration of the coating process.

In 1970, the U.S. Environmental protection Agency introduced the Clean Air Act.[6] The hot-melt coating techniques have been shown to avoid the use of solvents and show promising for taste masking, gastric resistance, acid resistance, sustained release or bioavailability enhancement, based upon type of coating polymer.[7] The present study was performed to check the suitability of cow ghee (CG) as a sustained release (SR) hot melt coating agent (HMC) in combination with ethyl cellulose. To prevent the oxidation of CG, α tocopherol was used as antioxidant in the coating composition.

Materials

Aceclofenac was obtained as a gift sample from Aarti drugs Ltd. Tarapur, Thane. Sucrose, alfa tocopherol and ethyl cellulose were procured from Themis laboratories Mumbai, India. Cow ghee was obtained from Gourakshan Centre Amravati, India. Solvents and all other reagents were of analytical grade and were procured locally.

Method

Preparation of aceclofenac pellets

Aceclofenac and sugar syrup (33.3% w/v) were blended in a suitable bowl for 5 min and passed through 16 meshes to from extrudates. The wet extrudate charged in to rotary shaker pelletizer and the equipment was operated for 5 min at 200 rpm to produce drug pellets.[8] Pellets were dried at 60^0 C for three hours and then sifted to collect 16- 20 mesh fractions. Undersize and oversize pellets were rejected. Pellets of fraction 16- 20 mesh were coated cow ghee ethyl cellulose molten blend in a 12 inches diameter coating pan equipped with 4 radially arranged baffles and a system to heat pan. The HMC compositions were shown in table 1. CG was heated to 80^0 C and ethyl cellulose was dissolved in the molten ghee with stirring at the same temperature. The aceclofenac pellets were then rolled in the coating pan until a bed temperature of 60^0 C was attained. The molten coating mass was loaded on to the hot rolling drug pellets in a slow stream. After the complete application of coating mass, the pellets were allow to roll further for 10 min during which time the bed temperature was allowed to gradually come down. The pellets were then removed and cured in dryer for 48 h. The parameters employed for HMC of aceclofenac pellets in coating pan are given in Table 2.

Table 1. Composition of sustained release hot melt coated aceclofenac pellet formulation

Formulation code	AC(mg)	α-tocopherol(mg)	Sucrose (mg)	Cow ghee (mg)	Ethyl cellulose (mg)
F1	200	40	24	00	01
F2	200	40	18	6	01
F3	200	40	9	9	01
F4	200	40	6	18	01
Total weight of pellets in each capsule			265 mg		

AC : Aceclofenac

Table 2. Process parameters for HMC of AC pellets

Process parameters	**Settings**
Pellet charge	500g
Pellet size	16- 20 mesh
Pan speed	24rpm
Amount of coating solution	50g
Core to core ratio	10.1
Pellet bed temperature	60^0 C
Relative humidity	30-50 %
Coating time	30 min
Curing conditions	30^0 C for 48 h

HMC: Hot melt coating, AC: aceclofenac

Evaluation of pellets

Physical characteristics

Table 4. Characterization of physiochemical parameters for coated aceclofenac pellets

Formulation code	**Mean Particle size (µ)**	**Hardness* (kg/cm^2)**	**Friability (%)**	**Drug content *(%)**
F1	830-890	2.65±0.001	0.73±0.003	99.56±0.004
F2	885-956	3.89±0.003	0.58±0.003	99.23±0.005
F3	852-923	3.71±0.002	0.60±0.003	98.87±0.004
F4	910-983	3.93±0.003	0.55±0.002	98.56±0.005

***Value (mean ± standard deviation) when sample size *n*=3**

Size determination was carried out using sieve analysis method. Approximately 200 g of pellets was placed into a sieve shaker equipped with standard test method sieves (14, 16, 18 and 20 mesh) for 5 min. The size distributions of pellets express the efficiency of the process of manufacture the uniform size pellets. The mean pellets size was calculated and recorded in Table 4.

Photomicrography

The morphology of pellets were studied by scanning electron photomicrograph (SEM) (FEE Philips – XL -30, VNIT, Nagpur) was performed to characterize the surface of the pellets. The results are shown in fig. 1 for coated pellets and in fig. 2 for uncoated pellets.

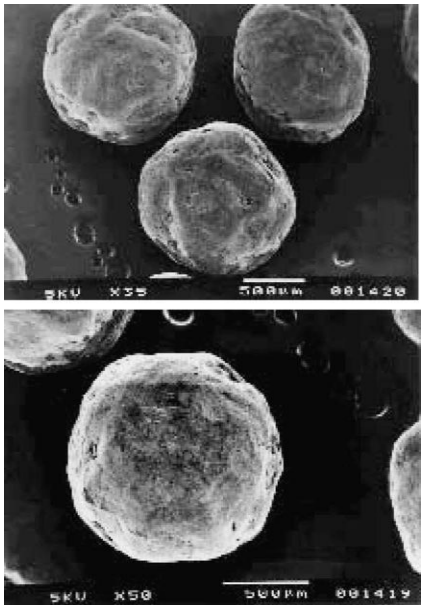

Fig. 1. Scanning electron photomicrographs of coated Aceclofenac pellets.

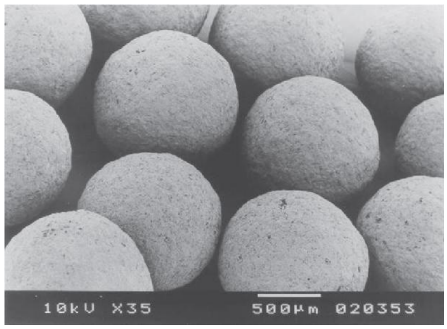

Fig.2. Scanning electron photomicrographs of uncoated Aceclofenac pellets.

Determination of drug content

An accurately weighed portion of pellets, equivalent to about 25 mg of Aceclofenac was transferred to 50ml volumetric flask, containing methanol, sonicated for 15 min and diluted up to the mark with methanol to get the desired concentration. The U V absorbance of the solution was determined at 278 nm. The percent drug content was calculated.[9]

Angle of repose

Accurately weighed 50g of HMC pellets were poured gently through glass funnel on the graph paper. The height of the pile and diameter were noted for determination of angle of repose. The values of angle of repose were recorded in Table 3. [10]

Table 3. Characterization of physiochemical parameters for coated aceclofenac pellets

Formulation code	Angle of repose* (0)	Bulk Density * (g/cc)	Tapped density * (g/cc)	Hausner's ratio*	Carr's Index * (%)
F1	25.32±013	0.65±0.001	0.75±0.003	1.12±0.004	9.86±0.036
F2	23.23±0.02	0.69±0.003	0.76±0.003	1.10±0.005	8.76±0.287
F3	21.32±0.02	0.71±0.002	0.77±0.003	1.09±0.004	8.10±0.351
F4	21.54±0.25	0.73±0.003	0.78±0.002	1.06±0.005	7.56±0. 412

***Value (mean ± standard deviation) when sample size *n*=3**

Bulk density

Accurately weighed 25g of HMC pellets of 16/20 mesh were poured gently through glass funnel in to 100 ml calibrated measuring cylinder. The surface was carefully made smooth without application of pressure. The volume occupied by sample was recorded and bulk density (g/cm) was calculated and recorded in Table 3.[10]

Tapped density

Tapped density was determined in a similar way to that of bulk density. However, final volume was measured afer tapping the cylinder from 3 inches until constant volume was obtained using Electrolab tapped density apparatus. The volume occupied by sample was recorded and tapped density g/ml was calculated and recorded in Table 3.[10]

Compressibility index

The morphology of pellets and total structure can change in any variation in formulation, affecting porosity, which is considered to have great influence on coating, flow and packing during tablet and capsule filling. It also influences the rate of release of drug from pellets by affecting the capillary action of dissolved drug. From the bulk density and tapped density data, the compressibility index was obtained and recorded in table 3.[10]

Hauser's ratio

From the bulk and tapped density data Hauser's ratio was obtained. Hauser ratio for the HMC pellets was carried out and recorded in Table 3.[10]

Hardness and friability

The hardness or crushing strength of HMC pellets was examined by Veego digital dial type hardness tester (Veego Scientific, India) and recorded in Table 3. For the friability study accurately weighed 10.0g pellets (initial weight) were placed on sieve having 0.85 mm aperture with 25 glass beads of 3mm diameter and then both were placed in Electrolab's friabilator (Electrolab, India) for 100 revolutions at 25 rpm speed. The pellets were collected and placed on the sieve with 0.85 mm aperture. The smaller particles were allowed to pass through the sieve and pellets were reweighed (Final weight). The friability was determined as percentage loss of mass of pellets after test was recorded in Table 4.[11]

In vitro drug release from pellets

In vitro release of aceclofenac pellets was carried out to evaluate the SR characteristics imparted by HMC with CG formulations. Dissolution studies were performed using USP XXV apparatus II, model Electrolab, 6 vessel assembly at 100rpm. The dissolution medium consisted of 750 ml of hydrochloric acid (pH 1.2) for 8 hours. Temperature was maintained at 37 ± 0.5^0 C. Aliquots of 5 ml were withdrawn at predetermined intervals and equivalent amount of fresh dissolution fluid equilibrated at the same temperature was replaced. Aliquots withdrawn were diluted suitably, filtered and analyzed spectrophotometrically at 278 nm. All release studies were conducted in triplicate and the mean values were plotted. The cumulative drug release against time was plotted in Figure 3.

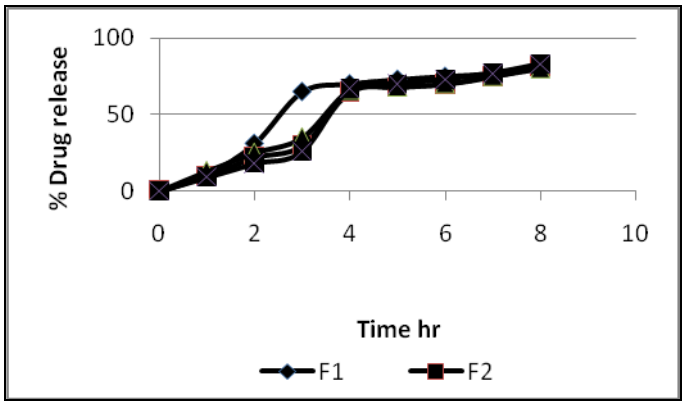

Fig. 3. In vitro release profile of aceclofenac from hot melt coated pellets

Stability studies for pellets

The pellets filled hard gelatin capsule shells were placed in amber coloured bottle and wrapped in aluminum foils. They were subjected to store at temperature $40^0 \pm 2^0$ C and relative humidity (RH) 75± 5% for six month in the stability chamber (Remi Laboratory Instrument CHM-6S GMP). The pellets were evaluated for any changes in physical appearance and percent cumulative drug release. After 6 month for stability study the results of drug release were plotted in Figure 4.

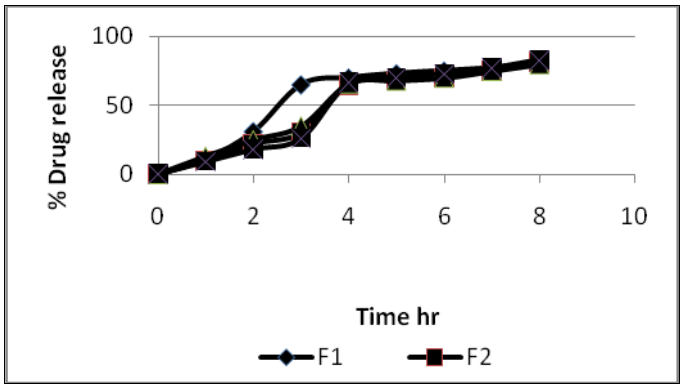

Fig.4. In vitro release profile of aceclofenac from hot melt coated pellets for stability study sample after six month

Results and Discussion

Hot-melt coating has been adopted because it is faster and cheaper than the conventional coating techniques where evaporation and/or recovery of solvent can be expensive, tedious and time consuming. Pellets with good surface morphology and smooth texture were produced in combination with cow ghee and ethyl cellulose using HMC technique. Scanning electron photomicrograph confirmed smooth and uniformity of coating of pellets (Figure 1.). Percent yield of coated pellets was found to be excellent since no agglomeration was observed during the coating. Hot melt coating established the simplicity and rapidity of processing and ease in the process. The evaluation parameters indicate that the pellets have good flow property with low frability and pass the test as per USP limits. The drug content in the prepared pellets was found to be within pharmacopoeia limit.

The selected optimized formulation was confirmed by comparing release profile. Drug release from aceclofenac pellets was clearly observed to be function of physiochemical property of the drug. The release profile results demonstrated more than 65% release in 4 hours. Since the method used for HMC did not facilitate more than 10% of coating composition, further retardation of aceclofenac release could not be achieved. The results of the significance determination were revealed that the kinetic parameter calculation demonstrated that the rate of dissolution fallows zero order kinetics.

Table 5. Kinetic parameters of formulations

Formulation code	Zero order model		First order model	
	Rate constant (k_0)	Correlation coefficient (R)	Rate constant (k)	Correlation coefficient (R)
F1	10.4521	0.9658	0.0764	0.9956
F2	8.324	0.9756	0.0864	0.9925
F3	3.512	0.9836	0.0231	0.9958
F4	4.865	0.9859	0.0465	0.9823

k_0 : Zero order rate constant , k: First order rate constant

The stability study demonstrated there was no significant change in physical characteristic and drug release pattern from pellets. Thus the aceclofenac prepared pellets were stable at accelerated condition. Thus, the percent composition of CG could be successfully employed as SR HMC agent as any other waxy material like Compritol.[12] If the amount of coating material deposited on the pellets could be controlled depending on the physico-chemical characteristics of the drug. Application of larger quantity of coating material could be made possible by use more sophisticated equipment and procedure like fluid bed coating.[13]

Conclusions

The objective of the present study was to design the SR hot melt coated aceclofenac pellets using CG in conjunction with ethyl cellulose as HMC agent. Since alone CG cannot provide physical strength and uniform thickness to the coating film Ethyl cellulose along with CG provide the strength as well as stability. The aceclofenac pellets were successfully prepared by HMC technique. The aceclofenac pellets prepared by this method were spherical in shape and had relatively smooth surface. The aceclofenac pellets were coated with CG using hot-melt coating technique was successful. Hot-melt coating technique presents a faster and cheaper alternative compared to conventional coating methods where solvent evaporation and recovery could become very expensive and time consuming. Dissolution study on the coated aceclofenac pellets showed that the release rate could be controlled using appropriate CG as a coating materials.

References

1. K. Lehmann, H. U. Petereit, D. Dreher, Drug Made Ger. 37 (1994) 53-60.
2. G.S. Rekhi, Pharm. Technol. 3 (1989) 112–125.
3. I. Ghebre-Sellassie, Drug Dev. Ind. Pharm. 11 (1985) 1523– 1541.
4 M.P. Flament, Pharm. Tech. Eur. 2 (1994) 19– 25.
5 M. Donbrow, M. Friedman, Drug Dev. Ind. Pharm. 4 (1978) 319–331.
6 Environmental Protection Agency. Clean Air Act. 1970.
7 P.H. Barthelemy, J.P. Laforet, N. Farah, Eur. J. Pharm. Biopharm. 47 (1999) 87– 90.
8 Jaiswal S.B. Studies on pelletization techniques. Ph.D. thesis, Faculty of Pharmaceutical Sciences. Nagpur, India: Nagpur University, 1995.
9 Golhar M.K., Joshi R.R., Gupta K.R., Wadodkar S.G. Int. J. ChemTech Res 2011, 3(2), 786-790.
10 Patil A.T, Chafle S A,Khobragade D S, Umathe S N, Avari J. Evaluation of hot-melt coating as taste masking tool. Int. Res. J Pharm 2011: 2:169-172.
11 Gandhi R, Lal Kaul C, Panchagnula R. Extrusion and spheronization in the development of oral control release dosage forms, Pharm. Sci Technio Today 1999; 4: 160-167.
12 Ke WT, Hsu TT, Hsiu O, Sheu MT. Physical and clinical characterization of ambroxol withcompritol 888 ATo. Asian J Pharm Sci 2006; 1: 35-42.
13 Sinchaipanid N, Junyaprasert V, Mitrevej A. Application of hot-melt coating for controlled release of propranolol hydrochloride pellets. Powder Technol 2004; 141: 203-209.

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