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INFLUENCE OF NATURE OF CORE ON NAPROXEN RELEASE FROM MICROCAPSULES

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ABSTRACT

Microcapsules are designed to obtain sustained release of naproxen. Investigations were conducted to evaluate the influence of the nature of core on the release of naproxen from ethyl cellulose microcapsules. Emulsification and solvent evaporation approach is employed to prepare the ethyl cellulose microcapsule of naproxen. When pure drug naproxen as such is employed to prepare the microcapsules – it resulted in very slow release in the first 2 hours in simulated gastric fluid and latter release was faster in the simulated intestinal fluid. This could be because of the difference in dissolution of the drug in the different fluids. But when naproxen gelucire dispersions were employed the release could be better controlled and was spread over a period of 12 hours. Two different types of gelucire are employed – gelucire (50/13) and gelucire (43/01). Solid dispersion of naproxen in gelucire (50/13) and gelucire (43/01) resulted in fast dissolving and slow dissolving forms of naproxen respectively. The various microcapsules were characterized with respect to drug polymer interaction, surface nature and drug release. The various microcapsules were found to be spherical and free flowing. The release was dependent on the nature of gelucire employed and the per cent coat of ethyl cellulose in the microcapsules. The release was found to follow first order kinetics and is diffusion controlled. It can be concluded from the results that release of naproxen from microcapsules can be modified by suitably altering the nature of naproxen that is incorporated as core in the microcapsules.

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INTRODUCTION

Naproxen is a non-steroidal anti-inflammatory drug (NSAID) commonly used for the reduction of moderate to severe pain and inflammation and stiffness. Naproxen has been proved to be effective in both experimental and clinical pain like rheumatoid arthritis, osteoarthritis, juvenile arthritis and acute gout. The usual dose of naproxen is 25-500 mg administered twice daily. The recommended adult dose of extended release naproxen tablets is 750 – 1000 mg once a day [1]. For ensuring optimal therapy with naproxen – it is recommended that patients receiving naproxen twice daily may be switched over to an extended release preparation by replacing their total daily total dosage with an equal dose of sustained/extended release formulation and then administered once daily. Naproxen is absorbed more than 95% after oral dosing but as it is practically insoluble in water sufficient plasma concentrations may not be built up to promptly initiate therapeutic response [2]. The desired pharmacodynamic activity of a once-daily dosage form of naproxen requires rapidly available naproxen for a prompt onset of analgesic activity, as well as a prolonged phase of absorption to provide 24-hour analgesic/anti-inflammatory activity [3].

But however administering a high dose of 750 mg (SR dose) in a tablet is fraught with risks of dose dumping. In this present investigation, we attempt to address the above 2 issues of low solubility of naproxen and design the sustained release form in multi - unit dosage form such as microcapsules from which the release is better controlled than from a single unit such as a tablet. There are reports of employing microcapsules] as sustained release dosage forms for various drugs [4-6]. But microcapsules of naproxen are not widely investigated for sustained release. Ethyl cellulose as a rate controlling polymers has received high attention in the preparation of microcapsules [7]. Design of sustained release products of drugs which have different extents of dissolution in the gastric and intestinal fluids is always challenging. Naproxen is a drug that shows slow dissolution in the gastric fluids and a rapid dissolution in the intestinal fluids. This problem of varying drug release due to the differing dissolution of naproxen is addressed in the present investigation. Instead of employing naproxen as such as a core in the microcapsules, a modified form of naproxen - a dispersion of naproxen - in gelucires - is employed.

Gelucires are a novel class of synthetic polymers derived from mixtures of mono-, di-, and triglycerides with polyethylene glycol (PEG) esters of fatty acids. Gelucires are available with a range of properties depending on their hydrophilic lipophilic balance (HLB 1-18) and melting point (33°C-65°C) range. The gelucires containing only PEG esters (Gelucire 50/13) are generally used in preparation of fast release formulations, while gelucires containing only glycerides or a mixture of glycerides and PEG esters (Gelucire 54/02, 43/01) are used in the design of sustained release formulations [8, 9]. Gelucires are selected as there are no reports on the feasibility of employing dispersions of drugs in gelucires in controlling the drug release from the microcapsules.

The major objectives of the present study are – a. to modify the drug dissolution by employing the dispersions of naproxen in gelucires and b. to prepare microcapsules loaded with modified forms of naproxen to obtain sustained release,. Such systems can be programmed to deliver at desired release rates – by altering the composition of core, coat and size of microcapsules. Also it is safer to administer the higher dose of drug from microcapsules rather than in the from a single matrix tablet.

MATERIALS AND METHODS

Materials

Naproxen is a gift sample from Julphar Gulf Pharmaceutical Industries, UAE, Gelucire (43/01) and Gelucire (50/13), are obtained from Genova Life Sciences, Bangalore, India.Ethyl cellulose. All other excipients, chemicals and solvents are of analytical grade and were purchased commercially.

Methods

Preparation of solvent deposited systems of naproxen

Solid dispersions were prepared by solvent method.

Solvent method

Solid dispersions of naproxen (N) in gelucire 50/13 (G) or gelucire 43/01 (Ge) were prepared in two ratios (N:G & N:Ge), 9: 1 and 4: 1. Naproxen (900 mg) was dissolved in 100 ml of methylene chloride. To the clear solution of the drug, gelucire (100 mg) was added and stirred to dissolve. Microcrystalline cellulose is added as fine particles The solvent is removed under vacuum and the mass obtained was scrapped and dried in a desiccator over anhydrous calcium chloride over night and was crushed, pulverized and sifted through mesh No. 100 and stored in a desiccator until further use.

Evaluation of solid preparations

Drug content uniformity

From each batch, four samples of 50 mg each were taken and analyzed for naproxen content. 50 mg of solid dispersion was weighed into a 50 ml volumetric flask. 40 ml of methanol was added and contents were thoroughly mixed to dissolve naproxen from the solid dispersions. The solution was made up to volume with methanol and suitably diluted with phosphate buffer of pH 7.4and assayed for naproxen content by measuring absorbance at 332 nm using phosphate buffer of pH 7.4 as blank. The results are given in Table 1

Dissolution studies

The dissolution of naproxen in pure form and from various solid dispersions was studied using USP Type II dissolution rate test apparatus (Lab India Model DISSO) employing a paddle stirrer. For dissolutions studies of dispersions in gelucire (50/13) were carried out in simulated gastric fluid and the dissolution studies of the dispersions in gelucire (43/01) were carried out in simulated intestinal fluid. In 900 ml of dissolution medium, a sample equivalent to 100 mg of naproxen was added and a speed of 50 rpm and a temperature of $37^{O}C \pm 1^{O}$ C were employed in each test. A 5 ml aliquot of dissolution medium was withdrawn at different time intervals, filtered, suitably diluted and assayed spectrophotometrically at 332 nm using Shimadzu UV spectrophotometer model 1800. The percent of naproxen dissolved at various time intervals was calculated and plotted against time. The results are given in Table 2 and shown in Fig.1 & 2

X-ray diffraction studies

X-ray powder diffraction patterns of naproxen and its solid dispersions were obtained by using X-ray powder diffractometer, PANalytical, (Model No X Pert Pro) with Xcelerator detector, employing Cu K_{α} radiation. The diffractograms were run between 2^{O} and 40^{O} at 2^{O}/min in terms of 2θ angle. The operation data were as follows: generator tension (voltage) 40 kV; generator current 30 mA. The diffractograms of naproxen and various solid dispersions are shown in Fig.3.

FTIR studies

Naproxen and the solid dispersions prepared were subjected to FTIR analysis using Fourier transform infrared spectrophotometer (Agilent Model Cary 630). Attenuated total reflectance (ATR) sampling interface was used to obtain the spectra. The IR spectra are shown in Fig 4.

DSC Studies

Naproxen and the solid dispersions were subjected to differential scanning calorimetric analysis to know about the physical state of the drug in the dispersion and any interaction between the drug and gelucire. The calorimeter (TA Instruments, Bangalore Model Q 20) was operated at a scanning rate of 10^{0}C per minute and heated between 25^{0}C to 250^{0}C. The samples were sealed in aluminum pans and heated in a constant inert atmosphere maintained by purging nitrogen gas at a flow rate of 10 ml/min. The thermograms obtained on various products are shown in Fig 5.

Preparation of microcapsules

Microcapsules were prepared by emulsification and solvent evaporation method. Naproxen as such or its dispersions were employed as core. Microcapsules were prepared in a core: coat ratio of 9:1 or 8:2. Ethyl cellulose (100 mg) is dissolved in 8 ml of acetone and the core (900 mg) – either naproxen or its dispersion in gelucires – is now dispersed the polymer solution. The resulting mixture is now added as a thin stream to liquid paraffin (agitated by Remi stirrer Model No. RQ 126 D) to disperse the added mixture as fine droplets. The mixture is agitated for 2 hours under vacuum to remove the acetone completely. The microcapsules with the rigidized coat are now separated by centrifugation and filtration. The microcapsules are then washed with petroleum ether and air dried to obtain discrete free flowing microcapsules. The details of various microcapsules prepared are given in Table 3.

Characterization of microcapsules

Size analysis

For the size distribution analysis, different sizes in a batch were separated by sieving employing a range of standard sieves and the amounts retained on different sieves were weighed.

Drug content

From each batch, four samples of 10 mg each of microcapsules were taken and analyzed for naproxen content. The weighed microcapsules were taken into a 50 ml volumetric flask. 40 ml of methanol was added and contents were thoroughly mixed to extract naproxen from the microcapsules. The solution was made up to volume with methanol and after filtration was suitably diluted with phosphate buffer of pH 7.4and assayed for naproxen content by measuring absorbance at 332 nm using phosphate buffer of pH 7.4 as blank. The results are given in Table 3

Scanning Electron Microscopy

The shape and surface features of the naproxen microcapsules were investigated by employing scanning electron microscope (SEM, Hitachi, Model SU 1510). The microcapsules were mounted onto the SEM sample stub and are observed under reduced pressure employing an acceleration voltage of 15 KV

Drug release studies

The drug release study from the various microcapsules was performed by employing USP Dissolution Rate Test Apparatus Type I employing a basket stirrer. The drug release study is performed in simulated gastric fluid for first 2 hours and in simulated intestinal fluid for the remaining 10 hours. Microcapsules equivalent to 500 mg of naproxen are taken for the study and samples of the medium are withdrawn at regular intervals and replaced by fresh medium and the absorbance of the filtered samples was measured at 332 nm. The results of the drug release study are given in Table 4 and shown in Fig 7.

RESULTS & DISCUSSION

The initial studies performed on the dissolution of pure drug naproxen in 0.1 N hydrochloric acid and in phosphate buffer of pH 7.4 revealed (Fig 1 & 2) that about 18% and 100% respectively was dissolved in one hour. The higher dissolution seen in phosphate buffer could be because of higher solubility of the drug in alkaline medium. However a slow dissolution in the acidic medium is a disadvantage and the release may be further hindered from a sustained release dosage form – particularly because the administered dosage form will remain for about 2 hours in the gastric fluids. This slow release in gastric fluids may not promptly build up the required plasma concentrations For a drug to be released from a dosage form, its dissolution in the dissolution fluids is a prerequisite. Thus, naproxen powder as such is unsuitable for preparing controlled release matrix tablets. So in the present work, a physically modified form of naproxen is prepared by solid dispersion of the drug in a water soluble carrier gelucire (50/13) to result in a more rapidly dissolving naproxen with the objective of verifying the feasibility of employing these dispersed forms of naproxen as a core in the microcapsules for achieving a faster but controlled release. Similarly the rapid dissolution of naproxen in phosphate buffer of pH 7.4 can also lead to rapid release of the drug from the microcapsules with no sustaining action. So a dispersion of naproxen – gelucire (43/01) which is found to be slow dissolving in phosphate buffer of pH 7.4 could be a better option to prepare the microcapsules with slow release of naproxen.

The dispersions of naproxen in gelucires as such yielded products which are a bit tacky and unhandable so the solvent deposited systems of the drug on microcrystalline cellulose were prepared. The solvent deposited systems of naproxen in the gelucires prepared by solvent method were found to be fine and free flowing powders. The percent drug contents of various solid dispersions are given in Table 1. There was no significant loss of drug during the preparation of solid dispersions and the proportion of drug and carrier remained the same as that initially taken. Low S.D. values in the percent drug content ensured uniformity of drug content in each batch.

Table 1 Naproxen Content of Various Solid Dispersions Prepared in Gelucires (50/13 & 43/01).

Solid dispersion	Mean ± s.d. (%)
Gelucire (50/13)	
N – G (9: 1)	90.12 ± 0.88
N – G (4: 1)	79.92 ± 0.17
N-G-MCC (8:2:2)	65.84 ± 0.21
Gelucire (43/01)	
N – Ge (9: 1)	89.88± 0.37
N– Ge (4: 1)	80.12 ± 0.35
N-Ge-MCC (8:2:2)	66.11 ± 0.25

The dissolution of naproxen (Fig 1) from its dispersions in gelucire (50/13) in 0.1N hydrochloric acid is found to be higher than the pure drug. This higher dissolution of naproxen from gelucire dispersions could be because the presence of drug in more amorphous form (as discussed below in the results of XRD analysis) and also because of the higher wettability of the drug in the dispersions. Whereas the dispersions in gelucire (43/01) exhibited slower dissolution (Fig 2) in phosphate buffer compared to the pure drug. This is because the drug is probably entrapped in a lipoidal matrix of gelucire (43/01) which hindered the free dissolution of naproxen. Also it is observed that the enhancing effect of gelucire (50/13) on the dissolution increased with higher amount of gelucire in the dispersion and also the retarding effect of gelucire (43/01) is also found to be more with the higher proportion of corresponding gelucire. Also it is observed that the naproxen is only partially converted into an amorphous form in gelucire (43/01) as evident from small endothermic peak obtained in its dispersions.

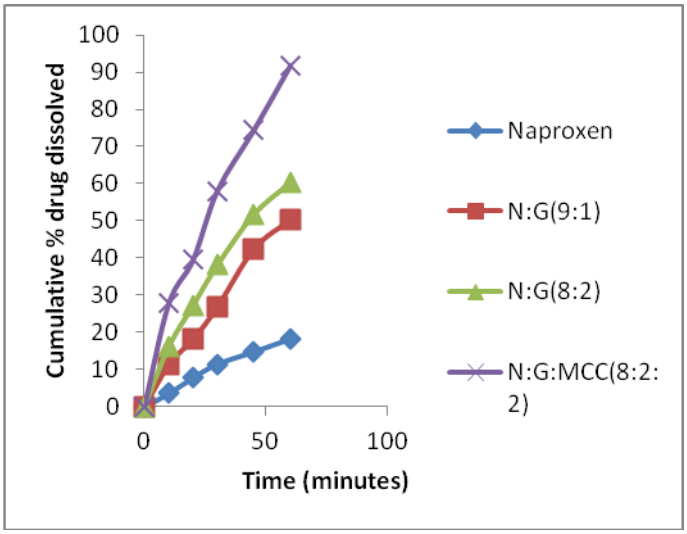

Fig 1 Dissolution profiles of various naproxen dispersions in gelucire (50/13) in 0.1 N hydrochloric acid.

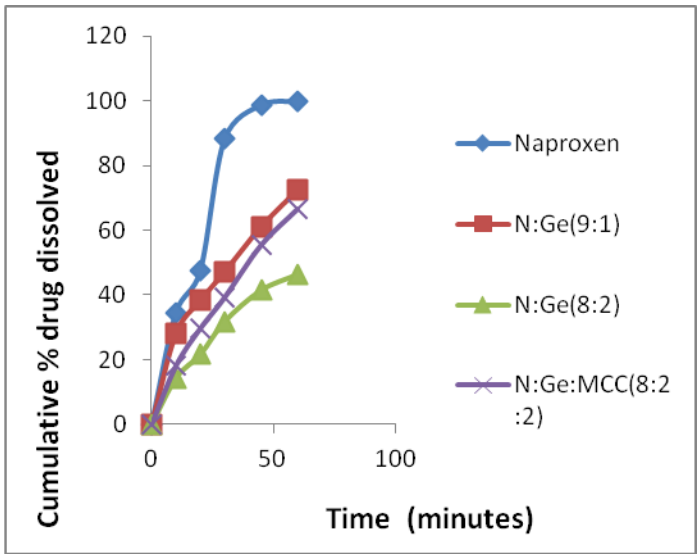

Fig 2 Dissolution profiles of various naproxen dispersions in gelucire (43/01) in phosphate buffer.

The various dissolution parameters are given in Table 2. It was observed that the dispersions in hydrophilic gelucire (50/13) showed higher dissolution rate constants and efficiency compared to the dispersions made with lipophilic gelucire (43/01). Thus from the dissolution studies it may be concluded that while gelucire (50/13) has promoted the dissolution rate of naproxen, gelucire (43/01) has retarded the dissolution. The dispersions deposited on microcrystalline cellulose gave free flowing powders of high dissolution rate because of significant increase in the surface area of the powders.

The usual method of evaluation of in vitro dissolution testing is the comparison of the time taken for given proportions of active drug to be released into solution and values such as T_{20}, T_{50} and T_{90} are often used. Another parameter suitable for the evaluation of in vitro dissolution has been suggested by Khan [10] **,** who introduced the idea of dissolution efficiency (D.E). D.E is defined as the area under dissolution curve up to a certain time 't' expressed as a percentage of the area of the rectangle described by 100 % dissolution in the same time.

Dissolution efficiency (D.E.) =

$$\frac{\int_0^t y\,dt}{Y_{100}\,t} \times 100$$

The dissolution efficiency can have a range of values depending on the time intervals chosen. In any case, constant time intervals should be chosen for comparison. For example, the index $D.E._{30}$ related to the dissolution of the drug from a formulation after 30 minutes could only be compared with $D.E._{30}$ of other formulations. Summation of the drug dissolution data into a single figure D.E., enables ready comparison to be made between a large numbers of formulations. The dissolution of naproxen in pure form and from various solid dispersions followed first- order kinetics. The dissolution plots are shown in Fig.1and 2 and data is given in Table 2.

Table 2 Dissolution Parameters of Various Solid Dispersions.

Solid dispersion	Dissolution efficiency (%) ± s.d	Dissolution rate constant (K_1) (min^{-1})	T_{50} (min)
Naproxen	5.27 ± 0.97	0.0023	> 60
N-G (9:1)*	11.45 ± 1.05	0.0115	57
N-G (8:2)*	21.67 ± 0.88	0.0138	45
N-G (8:2)*	33.85 ± 1.11	0.0345	26
Naproxen#	52.68 ± 0.91	0.0811	20
N-Ge (9:1) #	32.53 ± 0.79	0.0212	33
N–Ge (8:2) #	17.29 ± 1.12	0.0091	>60
N-Ge-MCC (8:2:2) #	24.16 ± 0.76	0.0161	40

* Dissolution data in 0.1 N hydrochloric acid.
\# Dissolution data in phosphate buffer of pH 7.4

X ray diffraction

The X-ray diffractograms of gelucires, pure drug naproxen and the dispersions are shown in Fig. 3. It is can be seen that the pure drug, which is highly crystalline as evident from the sharp diffraction peaks is converted into an amorphous form in the solid dispersions with gelucire (50/13), as the crystalline peaks have disappeared. It can also be noticed that the extent of reduction in crystallinity is less with the dispersion prepared by employing gelucire (43/01) Fig. 3 (C). So the increased dissolution of the drug from the solid dispersions is probably because of the crystalline drug naproxen being converted into an amorphous form and also because of the increased wetting action of gelucire (50/13) on the drug.

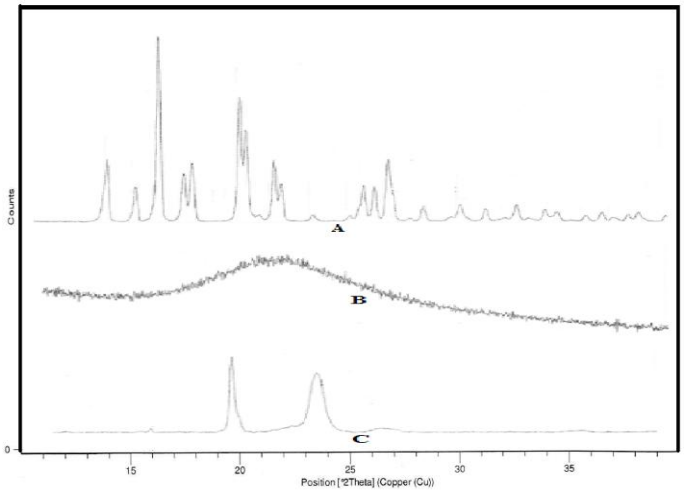

Fig 3 X-ray diffractograms of (A) Naproxen (B) Naproxen - gelucire - 50/13 Dispersion (C) Naproxen – gelucire – 43/01 Dispersion.

FTIR Studies

Any possible interaction between naproxen and the polymers – gelucires and ethyl cellulose – was verified by comparing the IR spectra of pure naproxen with that of dispersions and the microcapsules The IR spectra are shown in Fig 4. Pure naproxen (A) exhibited characteristic peaks due to carbonyl stretching vibration bands at; 2867.58cm^{-1} (–CH stretching vibrations (C-CH3) ;1728 cm^{-1}(–C=O stretching vibrations) ; 1393 cm^{-1} (OH deformation vibrations); 673.56 cm^{-1} (bending vibrations due to CH=CH). The solid dispersions (D & E) in gelucire (50/13 & 43/01) and the microcapsules (G) also exhibited the characteristic peaks of naproxen indicating retention of chemical identity of naproxen. Hence, there was no interaction between the drug and excipients used in the study.

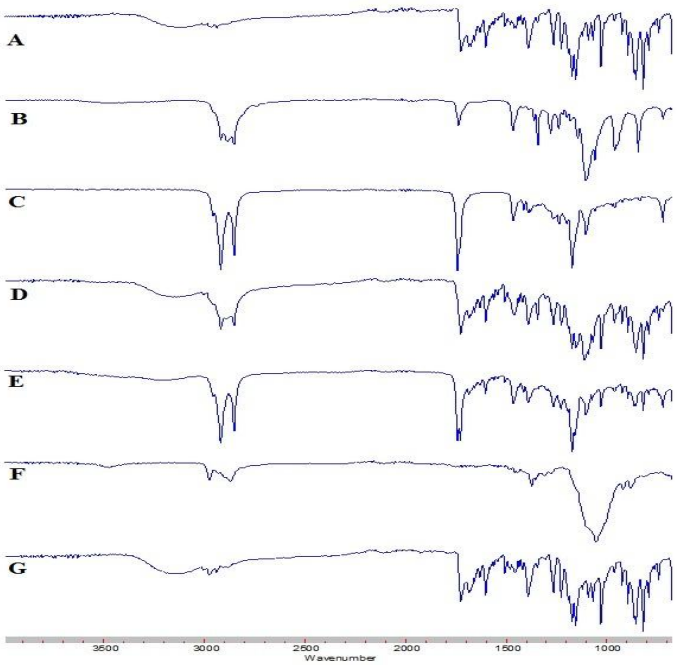

Fig 4 IR spectra of Naproxen and various products: (A) Naproxen, (B) Gelucire 50/13, (C) Gelucire 43/01, (D) Naproxen: Gelucire 50/13, (E) Naproxen: Gelucire 43/01, (F) Ethyl cellulose and (G) Naproxen: Ethyl Cellulose.

Differential Scanning Calorimetry

The thermograms of naproxen and the dispersions are shown in Fig 5. The endotherm of pure drug naproxen showed a sharp peak at 157^{o}C which is due to its melting point. Gelucire (50/13) showed its endothermic peak around 47^{o}C. Whereas the sharp endothermic peak expected of naproxen in the gelucire dispersions disappeared almost completely. This could be due to the presence of the drug in soluble amorphous state in the polymer and complete loss of crystallinity.This loss of crystallinity and presence in soluble state resulted in faster dissolution of naproxen from the gelucire solid dispersions. In case of the dispersion in gelucire (43/01), a small endothermic peak was observed at a lower temperature than the actual melting point of naproxen this could be because of the partial conversion of crystalline naproxen into an amorphous form in the lipophilic gelucire. This could be the reason for the slower dissolution of these dispersions in addition to the fact that the drug is dispersed in a lipophilic matrix of gelucire (43/01).

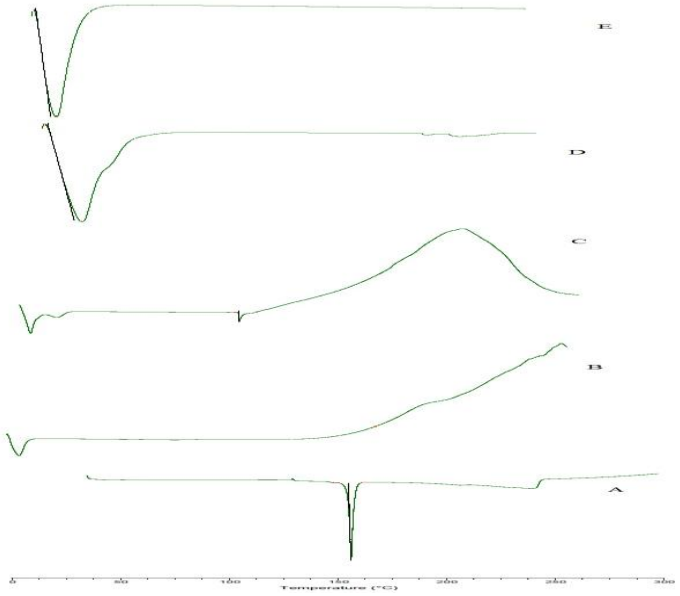

Fig 5 DSC thermograms of (A) Naproxen, (B) Naproxen – gelucire 50/13 , (C) Naproxen –gelucire 43/01 ,(D) Gelucire 50/13 and (E) Gelucire 43/01.

Characterization of Microcapsules

The microcapsules prepared were found to be discrete, spherical and free flowing. The sizes could be separated and a more uniform size range of microcapsules could readily be obtained. The size analysis of different batches of microcapsules showed that generally the size ranged from 300 to 1000 µ. It was observed that when the microcapsules were prepared employing higher proportion of coating polymer – it resulted in microcapsules of higher size. This could be because the higher amount of polymer – resulted in a more viscous dispersion and a bigger seed microcapsule being formed in the liquid manufacturing medium (liquid paraffin) into which the polymer solution and core mixture is slowly added as a thin stream. The details of different microcapsules prepared are given in Table 3. The drug contents of different batches of microcapsules found to be uniform. The SEM photographs of microcapsules shown in Fig 6 indicate that the microcapsules are nearly spherical and existed as discrete individual units but surface appears to be slightly rough in nature.

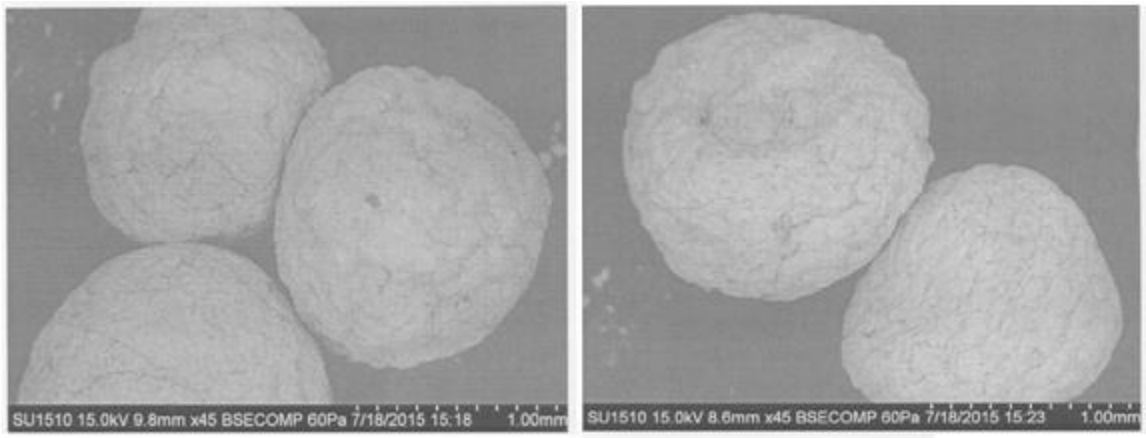

Fig 6 Scanning Electron Microscope images of naproxen microcapsules.

The various drug release profiles are shown in Fig 7. The microcapsules of pure drug naproxen (MC1) exhibited slow release in the first 2 hours but latter in the phosphate buffer the release could not be sustained as the drug is more soluble in alkaline fluids and even in the microcapsule form the drug release could not be controlled. When the N-G-MCC dispersion is employed as core in the microcapsules (MC2 & MC3) to overcome the very slow release that is seen in the first 2 hours, the release was higher than what is observed with microcapsules of pure drug but subsequently the release could not be controlled in the phosphate buffer as the drug from the core got released fast. When the N-Ge-MCC dispersion was microencapsulated (MC4 & MC 5), the release is retarded because the drug from the core which is mainly lipophilic could not get released. As the proportion of ethyl cellulose (coat) increased – the release of naproxen decreased in all types of microcapsules. While the microcapsules prepared by employing N-G-MCC dispersion could not sustain the release beyond 6 hours, the microcapsules prepared by employing N-Ge-MCC dispersion as core could release the drug only by about 69-79% by the end of 12 hours. So it is evident from the findings that the release of naproxen varied with changes in the percent coat material and also significantly with the nature of core that is employed in the preparation of microcapsules.

Table 3 Naproxen Microcapsules and their Drug Contents.

Microcapsules	Core	Core: Coat ratio	Mean ± s.d. (%)
MC 1	N	9:1	91.04± 0.33
MC 2	N-G-MCC (8:2:2)	9:1	59.84 ± 0.46
MC 3	N-G-MCC (8:2:2)	8:2	53.67 ± 0.27
MC 4	N-Ge-MCC (8:2:2)	9:1	60.24 ± 0.37
MC 5	N-Ge-MCC (8:2:2)	8:2	54.55 ± 0.31
MC 6	N-G-MCC (8:2:2) – 70 % and N-Ge-MCC (8:2:2) – 30 %	8:2	53.91 ± 0.11

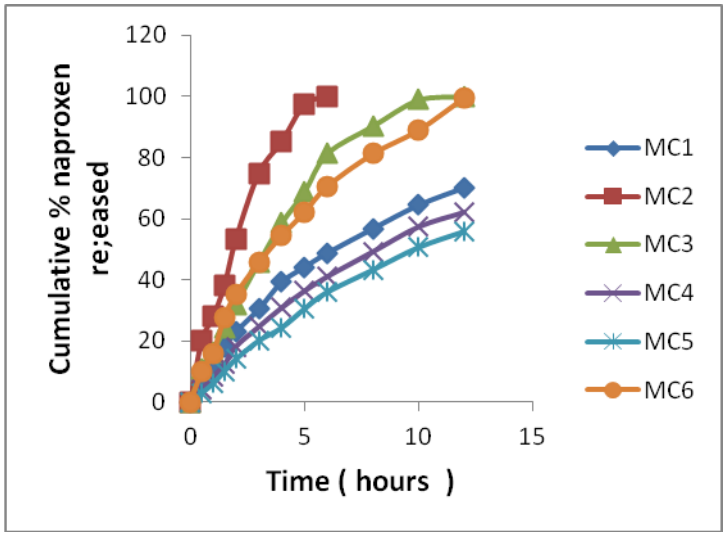

Fig 7 Naproxen release from various microcapsules.

So to obtain a drug release which is slow and spread over a period of 12 hours - a core comprising a combination of the dispersion in hydrophilic and lipophilic gelucires is employed. The core of such microcapsules (MC 6) consisted of 70% N-G-MCC and 30% N-Ge-MCC dispersions and the core to coat ratio is 8:2. It can be seen from Fig 7 that the release is neither very fast nor very slow in the first 2 hours and latter in the alkaline fluids as well the release is slow and uniformly spread over 12 hours.

To know the drug release mechanism – the data are analyzed as per zero order, first order, Higuchi [11] and Peppas [12] models. The model that best fits the release data was evaluated by correlation coefficient (r^2). The r^2- values in various models is given in Table 4. The plots of amount released versus square root of time were linear and the high r^2 values suggested the drug release is by diffusion. The correlation coefficient values were higher for first order model than zero order models indicating the drug release from the matrix tablets was according to first order kinetics. According to the n values (between 0.562 and 0.687), obtained in the Peppas plot, one may conclude that the drug release follows non-Fickian anomalous diffusion. Accordingly the drug release from these matrix tablets involves penetration by dissolution fluid, dissolution of the drug in dissolution fluid and diffusion of the dissolved drug.

Table 4 :Correlation Coefficient (r^2) Values in Various Kinetic Models and First Order Rate Constant of various Microcapsules.

Microcapsule	Correlation coefficient (r^2)				First order constant K_1(hr^{-1})	Peppas 'n' value
	Zero order	First order	Higuchi	Peppas		
MC1	0.857	0.982	0.954	0.967	0.322	0.562
MC2	0.871	0.977	0.94	0.965	0.166	0.687
MC3	0.899	0.986	0.939	0.992	0.131	0.545
MC4	0.847	0.969	0.966	0.988	0.292	0.572
MC5	0.912	0.979	0.964	0.952	0.175	0.631
MC6	0.937	0.980	0.948	0.993	0.124	0.674

CONCLUSIONS

Solid dispersion of naproxen in gelucire (50/13) and gelucire (43/01) resulted in fast dissolving and slow dissolving forms of naproxen respectively. When these dispersions were employed as core in the ethyl cellulose microcapsules – the release was dependent on the nature of the core employed. The release from microcapsules with the naproxen dispersion in gelucire (50/13) could not be sustained beyond six hours whereas the release from microcapsules with the naproxen dispersion in gelucire (43/101) was very slow. The release also varied with the amount percent coat (ethyl cellulose employed). When a combination of the 2 dispersions is employed as core, there is a more uniform retarded release which is spread over 12 hours. Of the various batches of microcapsule prepared – batch MC6 - is found to give slow and complete release. The findings of the present study suggest that modifying the core of microcapsules employing hydrophilic and hydrophobic gelucires is a promising approach to design sustained release products of poorly soluble drugs such as naproxen. Further research into the role of different other polymers on the release of naproxen from microcapsules is recommended.

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Authors' Statements:

Competing Interests

The authors declare no conflict of interest.

List of Abbreviations:

SR :	Sustained Release
HLB :	Hydrophilic lipophilic balance
N:	Naproxen
G :	Gelucire (50/13)
Ge:	Gelucire (43/01)
USP:	United States Pharmacopoeia
FTIR :	Fourier Transform Infrared Spectroscopy
DSC;	Differential Scanning Calorimetry
SEM:	Scanning Electron Microscopy
XRD:	X Ray Diffraction
D.E:	Dissolution Efficiency
MCC:	Microcrystalline cellulose
MC:	Microcapsule

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