Development and evaluation of eudragit based microparticles of dexibuprofen for site specific drug release

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Abstract: The main purpose of work was to formulate dexibuprofen loaded eudragit L-100 micro particles to acquire site specific delivery of dexibuprofen. Micro particles were formulated by an emulsion solvent evaporation method. Four formulations F1, F2, F3 and F4 having drug to polymer ratio 1:1, 1:2, 1:3 and 1:4, respectively were prepared and characterized. The rheological properties manifested that micro particles were worthy for further pharmaceutical exploitation. No notable drug polymer interaction was perceived in FT-IR spectroscopy. SEM micrographs showed rough surface of micro particles. The resulting micro particles had high entrapment efficiency greater than 70%. The *in vitro* dexibuprofen release at pH 1.2 exhibited poor drug release with less than 21% while at pH 6.8, 60% of the dexibuprofen was released up till 8th hour. The dexibuprofen release was modified by altering polymer concentration in the formulation. The subsequent micro particles were found to be best fit with zero-order release model. Micro particles were efficiently formulated with a focus to release the drug majorly in small intestine. With increase of polymer concentration enhanced entrapment efficiency and decelerated dexibuprofen release from the micro particles has been achieved. *In vitro* dexibuprofen studies verified the gastro-resistant property of micro particles thus qualify site specific release in gastrointestinal tract.

Keywords: Eudragit L-100, dexibuprofen, pH modulated micro particles, emulsion solvent evaporation, entrapment efficiency, FT-IR spectroscopy, *in vitro* drug release studies.

INTRODUCTION

Dexibuprofen is pharmacologically active enantiomer of Ibuprofen. Dexibuprofen shows fast action than ibuprofen and has significant therapeutic benefits over ibuprofen (Kumaresan, 2010). It is an effective NSAID in dental pain, dysmenorrhoea, postoperative pain, headache, sprains, and soft-tissue rheumatism, musculoskeletal and joint disorders (Sweetman Sean, 2009). Dexibuprofen is equally efficacious, safe & tolerable as celecoxib in the treatment of osteoarthritis (Phleps, 2001). Dexibuprofen is practically insoluble in water but soluble in alcohol, methanol, acetone, chloroform. It is well absorbed primarily from the small intestine. Its $t_{1/2}$ is 1.8-3.5 hrs, C_{max} is 22µg/ml & t_{max} is 2.5 hrs (Rehnasalim *et al.*, 2013). The most common adverse effects of NSAIDs are generally gastrointestinal ulceration after oral administration (Sweetman Sean, 2009). The underlying cause of gastric disturbances is combined effect of systemic prostaglandin synthesis inhibition & topical irritation of the drug (Musumba *et al.*, 2009).

Eudragit L 100 is biocompatible anionic copolymer of methacrylic acid & methyl methacrylate. It is resistant to gastric fluid. Eudragit is soluble in intestinal fluid at the pH >6 (Rowe *et al.*, 2009). The development of enteric micro particulate drug delivery system protects mucosa from NSAIDs induced ulceration (Gupta *et al.*, 2010). Enteric micro encapsulation is also done to improve the oral bioavailability of lipophilic drugs (Al-Ghananeem *et al.*, 2010). Various types of dexibuprofen formulation other than marketed conventional dosage forms were recently reported to enhance patient compliance like micro-beads of sodium alginate and hydrated sodium silicate having dexibuprofen (KMa *et al.*, 2012), prodrug of dexibuprofen-dextran (Rasheed *et al.*, 2009), sustained release matrix tablets of dexibuprofen (Selvadurai *et al.*, 2011) and dry elixir formulation of eudragit RS containing dexibuprofen (Kim *et al.*, 2011).

The aforementioned reports encouraged us to formulate, characterize and to evaluate pH modulated micro particles of dexibuprofen by emulsion solvent evaporation. The micro particles yield, drug loading and encapsulation efficiency, *in-vitro* release studies, FT-IR spectroscopic Studies, were investigated. The parameter that is polymer to drug ratio influencing the formulation of micro particles was also investigated.

MATERIALS AND METHODS

Materials

Dexibuprofen (SAMI Pharmaceuticals, Pakistan), eudragit L-100 (Sigma, United States of America), magnesium stearate and paraffin oil (Merck, Germany), ethanol, methanol, acetone and sodium hydroxide (NaOH) (Merck, Germany), potassium dihydrogen phosphate (KH_2PO_4) (Panreac Quimica SA, Barellona, Spain) and distilled water (Pharmaceutics Research Lab of the Islamia University of Bahawalpur, Pakistan) were used.

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Preparation of micro particles

Various solvents were investigated to select a suitable solvent system. Concentration of polymer, concentration of emulsifying agent, method of mixing and in process stability in the current method was also optimized. Less toxic solvents such as acetone, methanol and ethanol, alone & in binary mixture of different ratios were assessed.

As shown in fig. 1, dexibuprofen was dissolved in 5ml of acetone. Eudragit L-100 was added in varying ratio in 10 ml of Ethanol with continuous stirring until a clear solution was obtained. Drug solution was then added into polymer solution. 50mg of magnesium stearate was dispersed into liquid paraffin with continuous stirring at 700 rpm at 30ºC for 15 minutes. Here, magnesium stearate was used as anti-aggregating agent to prevent large agglomerates of micro particles. The resultant mixture of drug and polymer was added slowly into 100 ml of liquid Paraffin, while stirring at 700-800 rpm and 30°C. After evaporation of solvent, 30ml of n-hexane was added to the suspension of micro particles. Then, micro particles were separated by filtration. The residue was washed twice with 50ml of n-hexane & dried in oven for 24hrs.

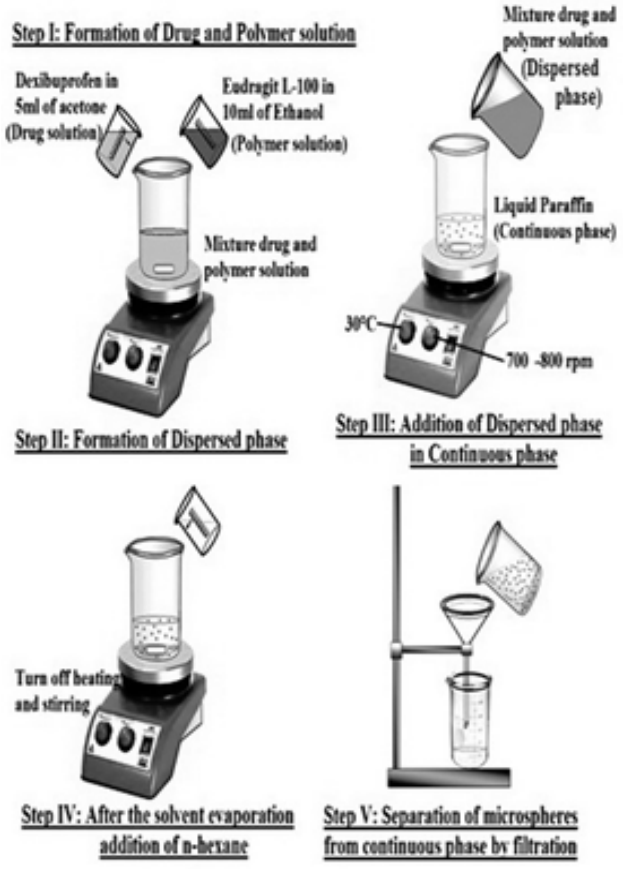

Fig. 1: Diagrammatic representation of micro particles preparation

In this study, we investigated the effect of increasing concentration of polymer on micro particles formation and its characteristics (table 1).

Table 1: Formulation code with their drug to polymer ratio

Formulation Code	Drug to polymer ratio
F1	1:1
F2	1:2
F3	1:3
F4	1:4

Characterization & evaluation of micro particles

FT-IR spectroscopic studies

Drug polymer interactions were studied by FT-IR spectroscopy. FT-IR spectra for drug (dexibuprofen), polymer (eudragit L-100) and dexibuprofen loaded eudragit L-100 micro particles of F1, F2, F3 and F4 having drug to polymer ratio 1:1, 1:2, 1:3 and 1:4, respectively were recorded in a fourier transform infrared (FT-IR) spectrophotometer (Bruker, Tensor-27, Germany). The Scanning range was 400-3500cm^{-1}.

Scanning electron microscopy

The surface morphology and appearance of micro particles were examined by scanning electron microscopy operating at 10kV. The micrographs were taken for 50-100µm micro particles sample. Micro particles were prepared by mounting on conductive carbon adhesive attached to alminium stub. Then, micro particles were coated gold to thickness of about 30nm using sputter coater. Then, micro particles were observed with scanning electron microscope (FEI, Quanta 250).

Production yield

The production yield of micro particles for each batch was calculated by using following equation.

$$\text{Production yield}\,(\%) = \frac{\text{Weight of drug loaded micro particles}}{\text{Total amount of drug and pleymer used}} \times 100 \quad (1)$$

Drug loading & encapsulation efficiency

100mg of accurately weighed drug loaded micro particles were added to 50ml of methanol and were stirred for 1 hour. The solution was then filtered with filter paper. 2ml of filtrate was diluted with 50ml of phosphate buffer (pH 6.8) & analyzed spectrophotometrically at 223nm by uv-visible spectrophotometer. The obtained absorbance was fitted in the equation of calibration curve to get the concentration of entrapped drug in micro particles. Then, dilution factor was multiplied with concentration to obtain actual drug contents in micro particles.

The drug loading & encapsulation efficiency (in percent) were calculated for each batch by using following equation 2 and 3.

$$\text{Drug Loading}\,(\%) = \frac{\text{Acrual Drug Contents in microparitices}}{\text{Weighed quantity of Microparticles}} \times 100 \quad (2)$$

$$\text{Encapsulation Efficiency (\%)} = \frac{\text{Acrual Drug Contents in Microparitices}}{\text{Theoretical Drug Contents in Microparitices}} \times 100 \quad (3)$$

In vitro drug release studies

Drug release studies were carried out on dexibuprofen loaded eudragit L-100 micro particles to study the effect of pH of dissolution medium. The release studies were performed using USP apparatus II (USP rotating paddle method). Accurately weighed micro particles were suspended in 500ml of dissolution media of pH 1.2 (i.e. 0.1 N HCl) and pH 6.8 phosphate buffer. The dissolution media were kept under stirring at 50 rpm and 37°C for 12 hours. At predetermined intervals, aliquots were withdrawn and replaced with respective dissolution media every time to maintain sink condition. After suitable dilution, samples were analyzed and estimated for dexibuprofen concentration at 223 nm spectrophotometrically (Shimadzu, UV-1601 UV-visible spectrophotometer). Dexibuprofen concentrations were calculated by using regression equation of calibration curve in following relationship.

$$y = 0.055x + 0.036 \quad (4)$$

Where, y is absorbance of sample, x is concentration of sample

Then, percent drug release was calculated by following relationship.

$$\text{Percent drug release} = Q_t/Q_{load} \times 100 \quad (5)$$

Where, Q_t is Amount of drug release at time 't', Q_{load} is Amount of drug loaded in micro particles.

The *in vitro* dexibuprofen release data were elucidated graphically using Graphpad prism 5 program by plotting the mean percent dexibuprofen release of each formulation with error bars extending to two standard errors at each *in vitro* release time points. Then, 95% confidence interval for the differences in the mean *in vitro* dexibuprofen release at each time point was evaluated.

Drug release kinetics

Various kinetic models were used to describe the release kinetics. Mathematical formulae were considered in the model dependent approach which explains the *in vitro* release data. At first, selection of appropriate model was done then *in vitro* release data was assessed according to derived parameters of model.

The release kinetics of dexibuprofen from eudragit L-100 micro particles was elucidated by applying following release kinetic models. (Mallapragada, 1999; Mulye and Turco, 1995; Bravo *et al.*, 2002; Chen *et al.*, 2007; Siepmann and Peppas, 2012)

Zero order kinetics: $Q_t = K_o t$ (6)

First order kinetics: $\text{Log } Q_t = \frac{\text{Log } Q_o + K_f t}{2.303}$ (7)

Higuchi model: $Q_t = K_h t^{1/2}$ (8)

Hixson crowel model: $Q_{o_{1/3}} - Q_{t_{1/3}} = K_{hc} t$ (9)

Korsmeyer- peppas model: $Q_t/Q_o = K_{kp} t^n$ (10)

Where, Q_t is Percentage of drug release at time't', K_o is Zero-order release rate constant, t is time, Q_o is Initial drug concentration, K_f is First-order release rate constant, K_h is Higuchi release rate constant, K_{hc} is Higuchi release rate constant, K_{kp} is Korsmeyer-Peppas release rate constant, n is release exponent which indicate the drug release mechanism and its values are given in table 2.

Table 2: Assessment of drug release mechanism

Release Exponent (n)	Drug Release Mechanism
0.5	Fickian Diffusion
0.45 < n > 0.89	Non-Fickian Diffusion
0.89	Case II Transport
> 0.89	Super Case II Transport

RESULTS

Characterization & evaluation of micro particles

FT-IR spectroscopic studies

FT-IR spectra of pure dexibuprofen, eudragit L-100 and dexibuprofen loaded eudragit L-100 micro particles of formulations F1, F2, F3 and F4 were investigated for chemical interaction between drug and polymer. FT-IR spectra of dexibuprofen, eudragit L-100 as well as formulations F1, F2, F3 and F4 were shown in fig. 2.

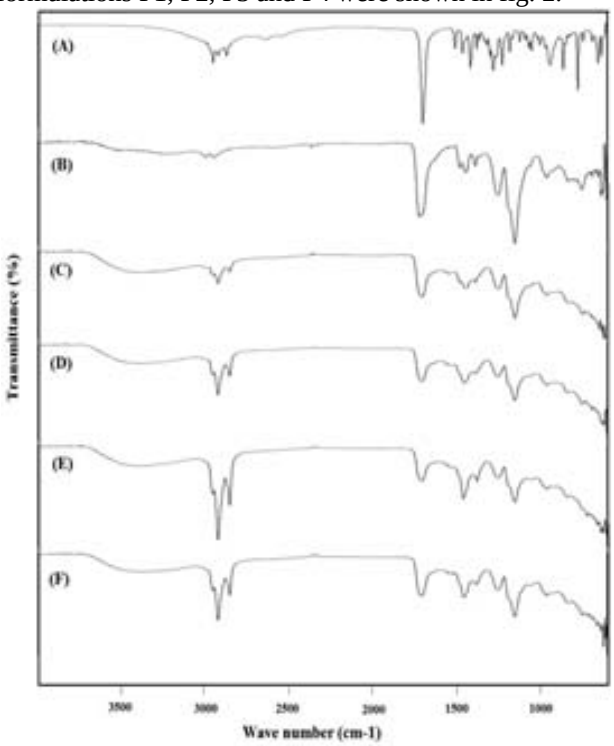

Fig. 2: FT-IR Spectrum of (A) Dexibuprofen, (B) Eudragit L-100, (C) F1, (D) F2, (E) F3 and (F) F4

Production yield, drug loading & entrapment efficiency

Production yield, drug loading and entrapment efficiency was determined and results are given in fig. 3.

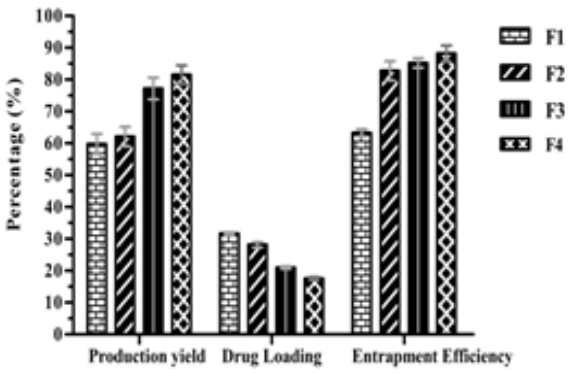

Fig. 3: Percentage of production yield, drug loading and entrapment efficiency in formulations F1, F2, F3 and F4, respectively

Scanning electron microscopy

Scanning electron micrographs of dexibuprofen micro particle formulation F2 are presented in fig. 4.

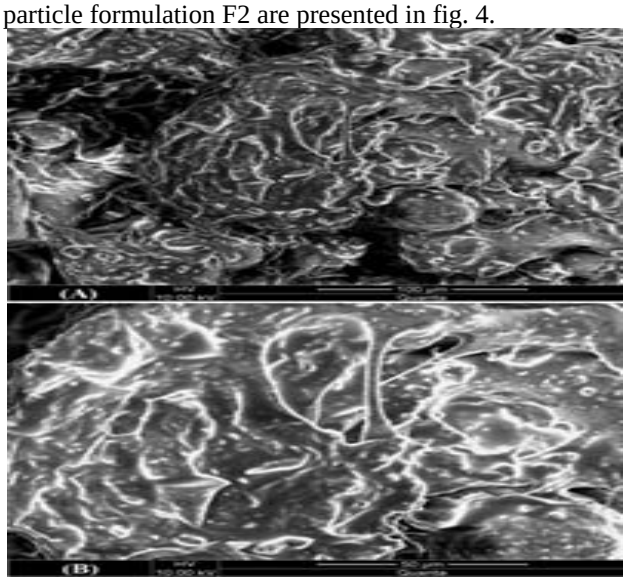

Fig. 4: Scanning electron micrographs of formulation F2

In vitro drug release studies

In vitro drug release studies was conducted at pH 1.2 & 6.8 as shown in fig. 5.

Drug release kinetics

Kinetic parameters of dexibuprofen release from eudragit L-100 micro particles at pH 6.8 are shown in table 3.

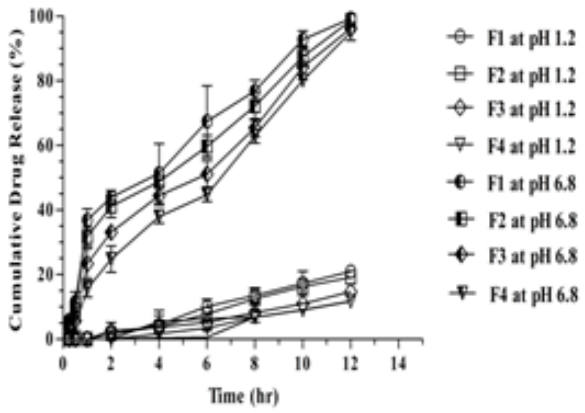

Fig. 5: Cumulative dexibuprofen release (%) of formulations F1, F2, F3, F4 having drug to polymer ratio (1:1), (1:2), (1:3), (1:4), respectively at pH 6.8 and

DISCUSSION

Any site-specific dexibuprofen formulation has not been reported yet so the present study is unique in this context. The rheological properties confirmed better flow and packing characteristics and suggested that micro particles could be easily handled.

Characterization & evaluation of micro particles

FT-IR spectroscopic studies

FT-IR spectra of all formulations were quite similar. The broad peak of hydroxyl group was appeared in range of 3398.81cm^{-1}-3412.32cm^{-1}. The peak of C=O stretch appeared in range of 1705.64cm^{-1}-1709.64cm^{-1}. The intense peaks of C-H stretch were appeared in range of 2853.26cm^{-1}-2922.58cm^{-1}. C-O stretching appeared in range 1153.11cm^{-1} - 1153.55cm^{-1}, C=C stretch showed in range of 1441.67cm^{-1}-1454.38cm^{-1} & C-H bending observed in range of 1251.80cm^{-1}-1253.41cm^{-1}. FT-IR spectroscopic results was suggested no considerable changes in FT-IR peaks but different transmittance (%) due to physical mixing of drug & polymer. It was clear

Table 3: Kinetic parameters of dexibuprofen release from eudragit L-100 micro particles of formulations F1, F2, F3, and F4 at pH 6.8

Model		F1	F2	F3	F4
Zero-order	K_o (%hr^{-1})	7.2951	7.2337	7.3355	7.4952
	R^2	0.9262	0.9421	0.9659	0.9874
First-order	K_f (hr^{-1})	0.0782	0.0839	0.0777	0.122
	R^2	0.662	0.6722	0.7187	0.6735
Higuchi	K_h(%$hr^{-1/2}$)	29.759	29.279	29.329	29.548
	R^2	0.9716	0.973	0.9734	0.9675
Hixon Crowell	K_{hc} (%hr^{-1})	0.1961	0.2038	0.1929	0.2424
	R^2	0.7686	0.7842	0.8406	0.8774
Korsmeyer-Peppas	n	0.7422	0.7852	0.8446	0.9174
	R^2	0.8985	0.9019	0.9262	0.9609
Mechanism of drug release		Non-Fickian transport	Non-Fickian transport	Non-Fickian transport	Super-case II transport

that the transmittance (%) of C=O stretch was decreased transmittance (%) of C-H stretch was increased due to physical interaction between drug and polymer. Therefore any possibility of drug polymer chemical interaction was ruled out as proved by FT-IR spectroscopic studies.

Scanning electron microscopy

Scanning electron micrographs of dexibuprofen micro particle formulation F2 revealed the surface morphology of micro particles. It was observed that micro particles were almost aggregated having rough texture (fig. 3).

Production yield

Irrespective of drug loading, the yield of micro particles was over 60% as shown in fig. 4. Production yield was low possibly because of polymer loss by adherence to the container or improper recovery of micro particles from the filter paper. Production yield was slightly lower when the concentration of polymer was less. By increasing the concentration of polymer from formulation F1-F4, increased production yield was achieved. In formulations F1 and F2, due to less polymer concentration smaller micro particles were obtained. These smaller micro particles were lost during the washing procedure resulted in low yield.

Shanmugarathinam *et al.* (2011) reported the similar results that when the ratio of drug to polymer increased the production yield was found to be increased from 72-84%. Maghsoodi (2009) reported the similar results that when the ratio of drug to polymer increased from 1:2 to 1:4, the production yield was found to be increased from 77-83% due to increase in particle size of micro particles.

Drug loading

Actual percentage of drug loaded in the formulations F1, F2, F3 and F4 was 50%, 33.33%, 25%, 20%, respectively. The drug loading of formulations F1, F2, F3 and F4 was 31.667±0.161, 28.183±0.351, 20.983±0.153 and 17.517±0.208, respectively. fig. 4 demonstrates the order of average drug loading of micro particles in different formulations was F1>F2>F3>F4. The results of drug loading revealed that the greater the proportion of drug in formulation, higher the drug loading.

Maghsoodi (2009) reported similar results that the average drug loading of naproxen containing eudragit L-100 micro spheres was increased by decreasing the drug to polymer ratio 1:4 to 1:1.

Entrapment efficiency

The entrapment efficiency of formulations F1, F2, F3 and F4 was 63.300%±0.458, 82.758%±1.212, 85.200%± 0.600, 88.167%±1.010, respectively. The order of entrapment efficiency of micro particles in different formulations was F4>F3>F2>F1 (fig. 4). The drug entrapment was enhanced significantly owing to increase in the polymer concentration with respect to drug progressively. Just as when the drug to polymer ratio was increased from 1:1 to 1:4.

This improvement in entrapment efficiency could be connected to the increasing proportion of polymer with respect to the amount of drug. When the concentration of polymer is increased viscosity of dispersed phase increased which can hinder the mobility of drug in droplet leading in entrapment efficiency. The underlying mechanism of this enhanced entrapment may be with increased concentration of polymer resulted in the faster precipitation of polymer on the droplet leading to faster solidification of micro particles which can obstruct the diffusion of drug and efficiently entrap the drug in micro particles.

Chinna *et al.* (2010) reported the similar results that when concentration of polymer was increased in eudragit L-100 micro spheres containing indomethacin, increase in entrapment efficiency was observed. This was attributed to the availability of increased polymer concentration to encapsulate indomethacin. Shanmugarathinam *et al.* (2011) reported similar results that entrapment efficiency was increased from 73%-83% by increasing the ratio of polymer from 1:3 to 1:6. Maghsoodi (2009) reported the similar results that naproxen entrapment efficiency was increased from 79% to 88.5% as drug to polymer ratio was increased from 1:2 to 1:4.

In vitro drug release studies

In the dissolution media of pH 1.2, strong release control and insignificant variation in drug release pattern was observed for micro particles (fig. 5). As the polymer is insoluble in the release media of pH 1.2, the micro particles were only slightly swollen but remain intact. At pH 6.8, the polymer was dissolved rapidly resulting in faster release of drug.

In-vitro dexibuprofen release profiles were not parallel and percent dexibuprofen release was significantly different at pH 1.2 and 6.8. These results clearly exhibited pH modulated release behavior of all formulations. Dexibuprofen release from micro particles of all formulations was less than 3% after 2 hours and less than 5% after 4 hours at pH 1.2. All formulations was also fulfilled the criteria of USP for enteric coated products. As USP stated that the enteric drug products should not release >10% of drug in first 2 hours at pH 1.2.

Shahzad *et al.* (2013) reported the similar results that eudragit L-100 micro spheres having greatest concentration of polymer concentration exhibited slower release at pH 1.2 and faster release at pH 6.8. Chinna *et al.* (2010) reported that swelling eudragit L-100 was very low in acidic medium resulting in less release of drug from micro spheres. The pH modulated release behavior

of eudragit L-100 was also reported by micro particulates of naproxen, indomethacin, celecoxib, flurbiprofen as well as prednisolone (Maghsoodi, 2009, Chinna *et al.*, 2010, Shahzad *et al.,* 2013, Najmuddin *et al.,* 2010, Kendall *et al.,* 2009). Therefore, eudragit L-100 proved to protect the drug from acidic environment.

Biphasic release behavior

The micro particles of formulations F1and F2 with drug to polymer ratio 1:1 and 1:2, respectively exhibited fast release followed by more constant release. However, this fast release is insignificant in formulations F3 and F4 with drug to polymer ratio 1:3 and 1:4, respectively (fig. 5).

As the greater concentration of polymer with respect to drug in formulation F4 may have been sufficient to entrap the drug. In case of dexibuprofen BCS class II drug, this fast initial release of drug is regarded functional in term of an initial dose during drug delivery followed by slower but continuous dose release of drug for the prolonged period of time. The fast release in the initial period probably due to dissolution and diffusion of drug stuck/lodged near to or at the surface of micro particles. While, slower release is accounted for diffusion of entrapped drug within the polymer. This excessive concentration of drug at the interface was responsible for the initial burst release. Therefore, very high drug loading fails the USP test for enteric coated micro particles.

Similar burst release behavior was observed in microcapsules of eudragit L-100 containing flurbiprofen. It was reported that this burst release behavior was linked to the presence of drug particles on the surface of microcapsules or improper drug encapsulation (Najmuddin *et al.,* 2010). Maghsoodi also reported the burst release behavior of eudragit L-100 micro particles at drug to polymer ratio 1:2. However this burst release was not seen in micro particles at drug to polymer ratio 1:3 and 1:4. It was attributed to greater concentration of polymer which completely entrapped all drug (Maghsoodi, 2009). Shanmugarathinam *et al.* (2011) reported that this burst release behavior of eudragit S-100 micro spheres containing aceclofenac due to the presence of drug particles on the surface of micro spheres.

Effect of varying drug to polymer on in vitro release profile

Cumulative release of formulations F1, F2, F3 and F4 having drug to polymer ratio 1:1, 1:2, 1:3 and 1:4, respectively strongly illustrated that release of dexibuprofen could be regulated by altering the polymer concentration. As seen in fig. 5, increase in the polymer concentration retarded the rate of dexibuprofen release from the micro particles. This retardation effect could be referred to an increase in particle size and hardening pattern of micro particles.

In the preparation of micro particles with high viscosity dispersed phase, polymer precipitation and its coagulation/drying were lagged. This was might be due to the penetration of more water into dispersed droplet before drying leading to the formation of greater water pores. More water pores facilitate the diffusion of dissolution medium into micro particles and consequently increase the drug release rate.

The particle size of micro particles is increased with an increase in concentration of polymer. The size of distribution of micro particles was slightly wider with an increase in polymer concentration. When the concentration of polymer is increased, the stirring efficiency is lessened resulting in the formation of large sized micro particles.

Increased drug concentration enhanced the concentration gradient between dispersed and continuous phase leading to enhanced partition of drug in the continuous phase. It can be understood that if high amount of drug was present in dispersed phase during solvent removal, it would precipitate leaving crystals of drug deposited on the surface of micro particles. This concept was significant in case of lipophilic drug, as the lipophilic drug crystals tend to gather at the interface of micro particle and liquid paraffin (Al-Ghananeem *et al.,* 2010). Chinna *et al.* (2010) reported the similar results that in eudragit L-100 micro spheres containing indomethacin, the rate and amount of drug release was observed to be decreased with the increase in polymer concentration. It was related to more binding of drug with polymer when the concentration of polymer was increased. Therefore, release of drug from the micro spheres was decreased.

Najmuddin *et al.* (2010) reported the similar results that flurbiprofen release was slowest from the micro spheres of formulation in which highest concentration of eudragit L-100 was present. As release of drug from eudragit L-100 micro spheres was depend upon swelling of polymer. Therefore, more time was required to swell the high concentration polymer. Similar prolonged release was observed in celecoxib containing eudragit L-100 because of good swelling characteristics of eudragit L-100 (Shahzad *et al.,* 2013). Maghsoodi (2009) reported the similar results that naproxen release was decreased with the increase of drug to polymer ratio (1:2 to 1:4). It was linked to increased diffusional barrier created by the polymer.

Drug release kinetics

Correlation coefficients (R^2) of all formulations is above 0.9 in Zero-order release model. Therefore, controlled release is the supreme mechanism of drug release.

By comparison of correlation coefficients (R^2) of Higuchi release model with Zero-order release model, First-order

release model, Hixson-Crowell release model and Korsmeyer-Peppas release model, it was clearly exhibited that in all formulations Higuchi model was best fit. Hence, the release of drug was controlled by molecular diffusion.

In Korsmeyer-Peppas release model 'n' is release rate exponent that exhibit the mechanism of drug release. The value of 'n' in formulations F1, F2 and F3 were greater than 0.7 (table 3) indicating the mechanism of drug release is non-fickian or anomalous transport. So, the drug release was regulated by both diffusion and dissolution. The dissolution of polymer matrix may be due to erosion and detachment of polymer. The value of 'n' in formulation F4 is 0.9425 indicated super-case II transport. In super-case II transport polymer swelling is occurred during the complete dissolution process. Swelling of polymer may be occurred in water and biological fluid. Above results suggested that more than one drug release mechanism may be involved.

Shahzad *et al.* (2013) reported the similar results that celecoxib release from eudragit L-100 micro particles followed Higuchi model. Based on the Korsemeyer-Peppas model concluded that drug release was non-fickian diffusion. Therefore, drug release was based on combined mechanism of erosion and diffusion. Maghsoodi (2009) reported that naproxen release from eudragit L-100 micro particles followed Hixson-Crowell model.

CONCLUSION

Dexibuprofen loaded eudragit L-100 micro particles were efficiently formulated with a focus to release the drug majorly in small intestine. It is believed to be more favorable in comparison with traditional drug delivery system. Incorporation of dexibuprofen in micro particles supposed to enhance the bioavailability. It is inferred that optimal formulation settings is vital for the enhanced entrapment efficiency and to modulate dexibuprofen release from the micro particles. *In-vitro* dexibuprofen studies verified the gastro-resistant property of micro particles, thus qualify the pH dependent release in gastrointestinal tract. *In vitro* studies could be decelerated by increasing polymer concentration. The dexibuprofen loaded eudragit L-100 micro particles had appropriate flow properties and were preferable to packed in the capsules. In future, *in-vivo* studies should be performed for dexibuprofen loaded eudragit L-100 to certify the enhancement of micro particulates drug delivery system.

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