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FORMULATION AND IN-VITRO CHARACTERIZATION OF SUSTAINED RELEASE MATRIX TABLET OF DEXIBUPROFEN

Abul Ashad Nistahar, Zubaidur Rahman*

NEF College of Pharmaceutical Education and Research, Nagaon, Assam, India.

Email: kazizubaidur1993@gmail.com

Keywords:

Dexibuprofen, FTIR, In-Vitro, Methyl Cellulose, Sustained Release Matrix Tablet.

ABSTRACT

Dexibuprofen is a Non-Steroidal Anti-Inflammatory Drug. It indicated for short term management of mild to moderately severe acute pain, along with dental pain, dysmenorrhoea, muscular pain and osteoarthritis. In the prevailing work, studies have been carried on the preparation and in-vitro characterisation of matrix tablets of dexibuprofen using different polymers like hydrophilic and hydrophobic. Different formulations had been prepared by wet granulation method using various release retarding polymers like methyl cellulose, xanthan gum and sodium carboxymethyl cellulose. Water soluble surfactant sodium lauryl sulfate had been employed for enhancing the solubility of the dexibuprofen. Drug-excipients compatibility became performed by way of FTIR. Different parameters had been evaluated for hardness, thickness, friability, drug content material and in vitro drug release. The excellent consequences were determined in terms of physico-chemical parameters. The 10 numbers of formulations have been discovered to display highest drug release of drug. Mathematical analysis of the release kinetics have been accomplished to determine the mechanism of drug release. In-vitro release records have been fitted into diverse models to envision the kinetic of drug release.

INTRODUCTION

Nonsteroidal anti-inflammatory drugs (NSAIDs) are contributors of a drug magnificence that reduces pain, decreases fever, prevents blood clots and reduces inflammation [1,2]. In standard, NSAIDs are characterised by way of a high degree of protein binding and small volumes of

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distribution [3]. In addition, dexibuprofen has verified comparable efficacy to diclofenac, naproxen and celecoxib [4]. Dexibuprofen is an S (+)-isomer of ibuprofen, which is a chiral spinoff of 2-arylpropionic acid and demonstrates comparable therapeutic behaviour to different non-steroidal anti-inflammatory drugs (NSAIDs). It has been set up that management of ~200 mg of dexibuprofen produces equivalent analgesic effects to ibuprofen, but with a lower possibility of manufacturing adverse gastric effects [5]. Dexibuprofen (Figure 1) belongs to BCS Class II of drug compound, because of its negative water solubility, which leads variability in drug absorption and erratic bioavailability. It is mainly used to control mild-to-moderate ache and inflammatory situations, including headache, postoperative ache, dysmenorrhea, dental ache and smooth tissue rheumatism [5,6]. A dose of 400 mg is effective to treat inflammatory situations, with the biologic half-life of dexibuprofen being 1.8–3.5 hours [7–9].

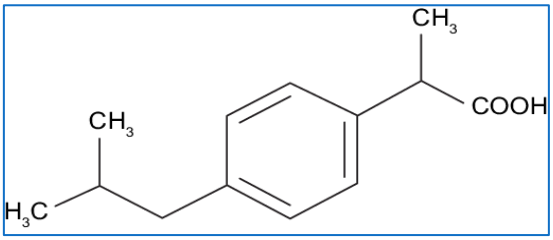

Fig 1: Chemical Structure of Dexiboprofen

Dextrarotatory isomer of ibuprofen dexibuprofen is the pharmacologically effective enantiomer, which turned into for the first time released in Austria in 1994 [10]. Racemic ibuprofen and dexibuprofen differ in their physical, chemical and pharmacological properties as well as their metabolic profile [11,12]. In the last 5 years, 4836 patients have been uncovered to dexibuprofen in clinical trials and post marketing surveillance (PMS) trials. Only in 3.7% of sufferers have adverse drug reactions been suggested and three extreme unfavorable drug reactions (0.06%) happened [11]. It has been demonstrated inside the in vitro version that dextrarotatory isomer famous approximately a hundred and sixty-instances better activity in prostaglandins inhibition in assessment to enantiomer (R). Other research of thromboxane technology in clotting blood also showed better activity of enantiomer S than racemate [13]. Therefore, it'd be tremendously fine to apply dexibuprofen as an ache reliver. Especially, due to the reality that whilst dexibuprofen efficaciously inhibits the activity of COX-1 and COX-2, the enantiomer (R) demonstrates the inhibition handiest in the direction of COX-1 and it's far really worth noting that it's miles accountable growing the aspect results in the gastrointestinal tract [14].

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The negative water solubility of a drug effects in low dissolution rate, with subsequent partial and inconsistent absorption, which limits the drug exposure at its active site and constrains its clinical effectiveness [15]. Additionally, poor patient compliance has been observed for drugs that are poorly water soluble due to the need to deliver higher doses, with consequent large unit dose sizes making them tough to swallow. This additionally will increase the cost of therapies and reduces their business elegance, even as the range in drug exposure typically related to products of this nature might have bad results and gain/chance profiles [16,17]. Generally available techniques for addressing problems of low aqueous solubility in pharmaceutical development consist of particle size reduction, micronization [18], hot melt extrusion technology [19], solid dispersions [18], nanoemulsions [19], microencapsulation [20], micelles [21], salt formation and complexation [22].

MATERIALS AND METHOD

Material:

Table I: List of Meterials Used

Sl. No.	MATERIALS	SOURCES
1	Dexibuprofen	Indian fine chemicals, Mumbai
2	Xanthan gum	Indian fine chemicals, Mumbai
3	Methylcellulose	Indian fine chemicals, Mumbai
4	Sodium CMC	S. D fine chemicals Limited, Mumbai
5	Micro-crystalline cellulose	Indian fine chemicals, Mumbai
6	Sodium lauryl sulphate	Merck specialities Pvt. Ltd, Mumbai
7	Magnesium stearate	Central drug house Pvt. Ltd, New Delhi
8	Talc	S. D fine chemicals, Mumbai
9	Sodium hydroxide	Fisher Scientific, Mumbai
10	Potassium dihydrogen phosphate	Qualigens fine chemicals, Mumbai

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METHOD

Formulation development in this work, wet granulation method was adopted with the aid of retarding agents for the preparation of sustained release matrix tablets of dexibuprofen. Development of the formulation in the present was mainly based on the type and concentration of polymers. Dexibuprofen tablets were manufactured by wet granulation method using polymers like xanthan gum, methylcellulose and sodium carboxy methyl cellulose (Sod. CMC). All the composition in Table 2 (except magnesium stearate and talc) were thoroughly mixed by mortar and pestle for a period of 15 minutes. The powder mixture was granulated with the required amount of alcoholic solution of ethanol. The wet mass was passed through sieve # 16 and the granules were dried at 50^{o}C for 2 hours in a hot air oven. The dried granules were passed through sieve # 20 and lubricated with magnesium stearate by further blended for 3 minutes and finally talc was added to the blend. The mixed blend of drug and excipients were compressed to produce convex faced tablets of 250 mg using 8 mm round punches on multipunch tablet compression machine. A batch of 50 tablets were prepared for each of the designed formulations.

Table 2: Formulation of Sustained Release Matrix Tablets of Dexibuprofen.

Ingredients	F1	F2	F3	F4	F5	F6	F7	F8	F9	F10
Dexibuprofen	50	50	50	50	50	50	50	50	50	50
Xanthan gum	50	100	-	-	-	-	-	-	-	-
Methylcellulose	-	-	50	100	-	-	50	100	-	-
Sodium CMC	-	-	-	-	50	100	-	-	50	100
Sodium lauryl sulphate	-	-	-	-	-	-	2.5	2.5	2.5	2.5
MCC	142.5	92.5	142.5	92.5	142.5	92.5	140	90	140	90
Magnesium stearate	2.5	2.5	2.5	2.5	2.5	2.5	2.5	2.5	2.5	2.5
Talc	5	5	5	5	5	5	5	5	5	5
Total(mg)	250	250	250	250	250	250	250	250	250	250

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Data Of *In Vitro* Drug Release Studies

Table 3: *In Vitro* Drug Release Profile of Dexibuprofen for Formulations F1 To F10.

Time (hrs)	Cumulative % of Drug Release									
	F1	F2	F3	F4	F5	F6	F7	F8	F9	F10
0.5	1.32	1.45	2.19	1.67	1.45	1.39	21.84	14.70	16.68	10.36
1	4.85	4.85	6.98	6.41	6.03	6.15	28.41	21.61	25.21	20.90
2	6.80	7.16	8.72	8.33	7.56	7.92	37.16	28.49	36.21	25.18
3	8.61	8.54	13.24	11.89	8.47	13.78	41.05	33.79	38.97	32.18
4	12.42	13.15	16.17	15.63	9.46	15.82	47.34	40.81	41.44	41.46
5	14.33	16.78	22.19	18.90	10.85	20.67	53.59	49.40	48.83	48.08
6	16.58	20.33	30.33	24.39	11.78	23.34	56.57	57.73	54.07	56.90
7	19.96	23.12	32.81	26.48	17.75	26.79	64.17	64.88	61.06	63.77
8	22.95	25.06	38.54	34.30	24.47	30.33	73.65	72.60	65.90	73.98
9	25.16	29.21	40.90	40.04	31.61	33.45	78.35	78.44	74.73	78.78
10	30.27	31.97	42.83	41.57	38.01	38.30	85.26	84.28	76.03	85.33
11	35.00	34.16	47.23	44.08	41.13	39.57	94.16	90.11	89.66	91.96
12	37.20	36.50	48.47	45.63	43.01	41.67	95.44	94.43	95.59	97.85

RESULTS

Pre-Compression Evaluation Parameters.

Physical Appearance:

Physical appearance of drug was examined by organoleptic properties and results are obtained as follows:

Colour: White or almost white.

Odour: Slight characteristic odour.

State: Crystalline powder.

The sample of dexibuprofen possess similar colour, odour, and texture as given in officials, this supports purity and authenticity of the drug.

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Determination Of Melting Point:

The melting point of the obtained sample was found to be 51ºC.

Determination of Solubility:

Table 4: Solubility of Dexibuprofen

SL. No.	Solvents	Solubility
1	Distilled water	Insoluble
2	Ethanol	Soluble
3	Methanol	Soluble
4	Phosphate buffer (6.8)	Slightly soluble

Infrared Spectral Assignment

The pellet of approximately 01 mm diameter of the drug was prepared grinding 3-5 mg of sample with 100-150 mg of Potassium Bromide using hydrostatic press. The sample pellet was mounted in IR compartment and scanned at wavelength 4000-500 cm^{-1}. The results were shown in figure 2.

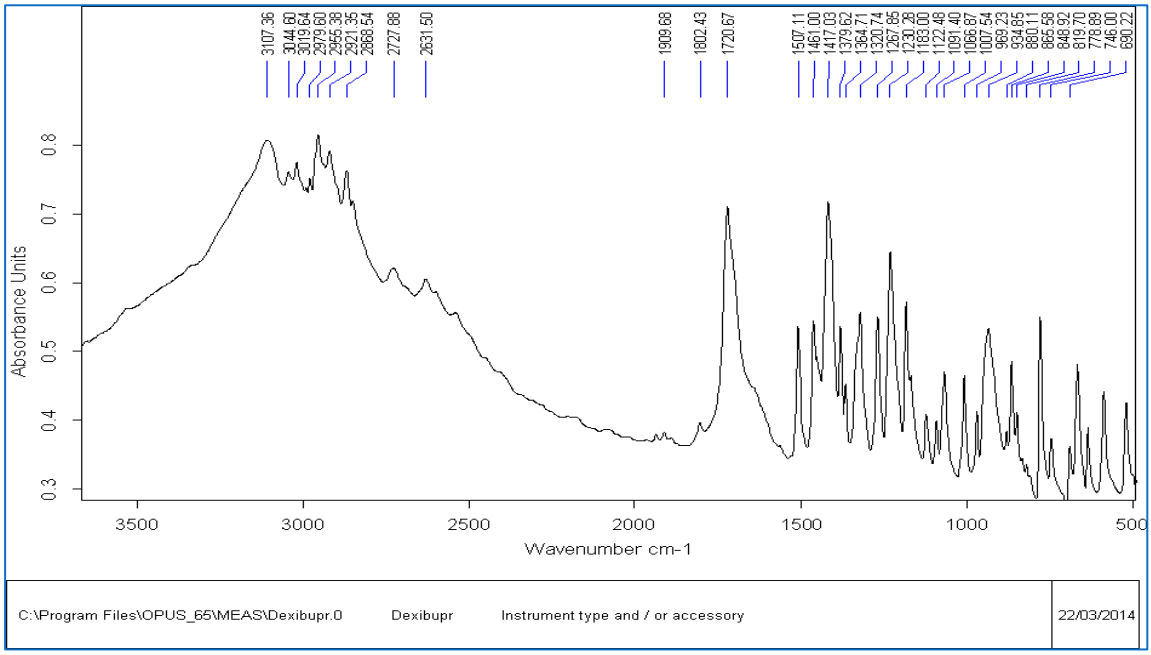

Figure 2: FTIR Spectra of Drug (Dexibuprofen)

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Table 5: Interpretation of Pure Dexibuprofen.

Functional Group	Wave Number (Cm^{-1})	Presence Of Peak
O-H Group	3107.36	Present
C-H Group	2955.38	Present
C=O Group	1720.67	Present
C-C Group	1417.03	Present
C-O Stretching	1230.28	Present
O-H Bending	778.89	Present

Ultraviolet Absorption Maxima

Ultraviolet absorption in the range of 200 to 400 nm of a 100 µg/ml solution of Dexibuprofen in phosphate buffer (pH 6.8) was scanned. The absorption maximum (λ_{max}) of Dexibuprofen was found be 222 nm which is shown in figure 3.

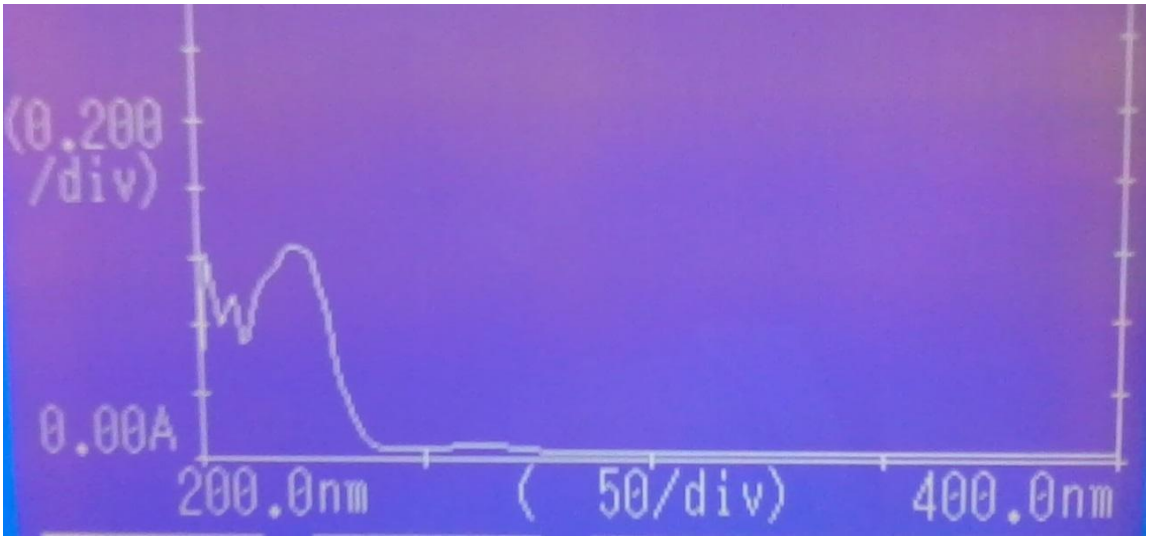

Figure 3: Scan of Dexibuprofen

Result Of Calibration Curvedata

The calibration curve of dexibuprofen turned into prepared in phosphate buffer (pH 6.8). The plot of various concentrations of dexibuprofen versus absorbance observed to be linear in the concentration range of 10-50 µg/ml at 222 nm. The absorbance at different concentrations was proven in Table 4. The statistics of preferred curve were linearly regressed. The slope and correlation coefficient values have been observed to be 0.0118 and 0.999 respectively. The calibration curve turned into proven in Figure 4.

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Table 6: Calibration Curve Data of Dexibuprofen

Sl. NO	Concentration (µg/ml)	Absorbance (nm)
1	0	0
2	10	0.124
3	20	0.245
4	30	0.356
5	40	0.465
6	50	0.601

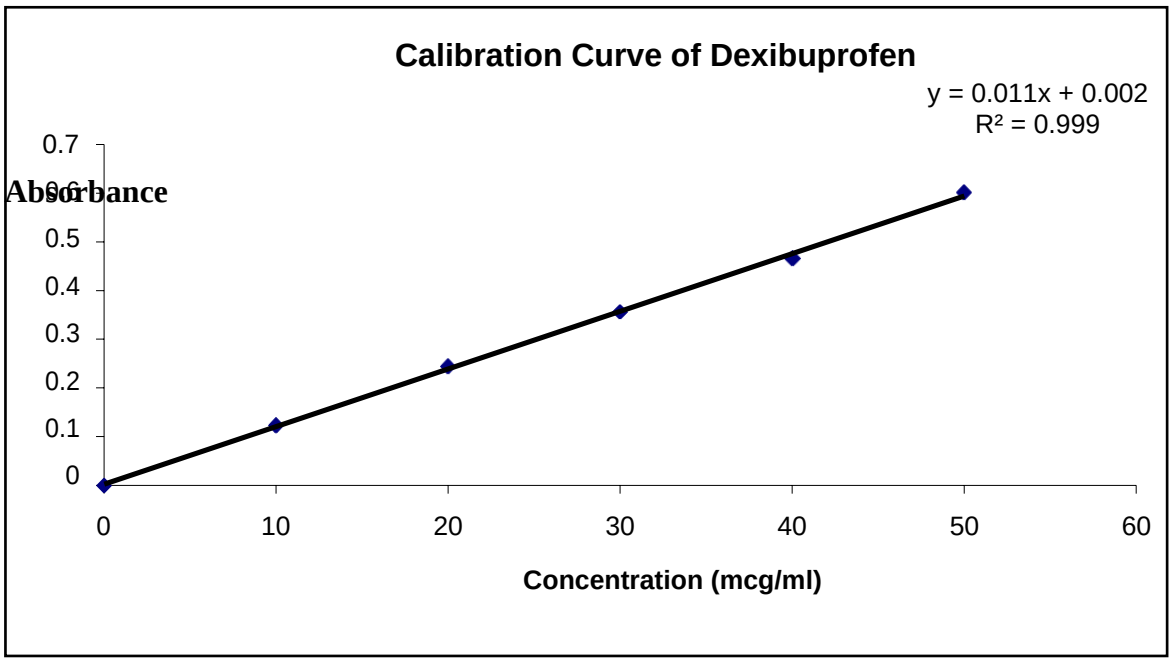

Fig 4: Calibration of Dexibuprofen

CONCLUSION

The objective of the present study became to formulate and examine sustained release drug delivery system for a non-steroidal anti-inflammatory drug. In this study, sustained release drugs were prepared with release retarding polymers and evaluate for numerous in-vitro parameters. Sustained release matrix tablets had been prepared by way of wet granulation technique the usage of distinctive polymers like xanthan gum, methyl cellulose, sodium CMC. Solubility of dexibuprofen became more advantageous by way of using water soluble surfactant SLS to acquire the preferred release. The tablets had been evaluated for his or her organoleptic (colour, odour), physical (size, shape and texture) and quality control parameters (thickness, weight variation, hardness, friability and in vitro release). Dexibuprofen was analyzed for spectral (FTIR, UV) properties. The received effects of

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dexibuprofen had been concordant with reference specs of FTIR. The outcomes showed that there was no interaction among the drug dexibuprofen and the polymers employed in the formulation. Among all the formulations F10 confirmed a higher drug release over 12 hours of time and it released over 97.95% of the drug out of 10 formulations with a sustained effect. Data of in-vitro drug release have been healthy into exclusive equations and kinetic model to give an explanation for the release kinetics of dexibuprofen from the sustained release tablet. On experimental records it turned into concluded that sustained release matrix tablets of dexibuprofen could be a powerful alternative technique for management of ache. Sodium CMC along with SLS turned into proved to be the maximum promising dosage shape for sustained release of dexibuprofen drugs. It became also found that there was no interection among the drug and polymer in all the formulations. Stability studies were conducted according to ICH guidelines, for excellent formula F10 for a length of 3 months and the acquired consequences have been in the specification at both refrigerator and Long-term conditions and out of specification at improved situation. Among all of the formulations, the optimized formula F10 fulfilled all the targets.

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CONFLICTS OF INTEREST: No

REFERENCES

1) Wu, D.; Bai, X.; Lee, P.; Yang, Y.; Windsor, J.; Qian, J. A systematic review of NSAIDs treatment for acute pancreatitis in animal studies and clinical trials. Clin. Res. Hepatol. Gastroenterol. 2020, 1, 1–18.
2) Fosslien, E. Adverse effects of nonsteroidal anti-inflammatory drugs on the gastrointestinal system. Ann. Clin. Lab. Sci. 1998, 28, 67–81.
3) Brater, D.C. Clinical Pharmacology of NSAIDs. Clin. Pharmacol. 1988, 128, 1121–1132.
4) Kaehler, S.T.; Phleps, W.; Hesse, E. Dexibuprofen: Pharmacology, therapeutic uses and safety. Inflammopharmacology 2003, 11, 371–383.
5) Kaehler S, Phleps W, Hesse E. Dexibuprofen: pharmacology, therapeutic uses and safety. Inflammopharmacology. 2003;11(4): 371–383.
6) Di Pierro F, Settembre R. Safety and efficacy of an add-on therapy with curcumin phytosome and piperine and/or lipoic acid in subjects with a diagnosis of peripheral neuropathy treated with dexibuprofen. J Pain Res. 2013; 6:497–503.
7) Eller N, Kollenz C, Schiel H, Kikuta C, Mascher H. Pharmacokinetics of dexibuprofen administered as 200 mg and 400 mg film-coated tablets in healthy volunteers. Int J Clin Pharmacol Ther. 1998;36(8):414–417.

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8) Zhang X, Liu X, Gong T, Sun X, Zhang Z-R. In vitro and in vivo investigation of dexibuprofen derivatives for CNS delivery. Acta Pharmacol Sin. 2012;33(2):279–288.
9) Evans AM. Comparative pharmacology of S (+)-ibuprofen and (RS)- ibuprofen. Clin Rheumatol. 2001;20(1):9–14.
10) Phleps, W. Overview on clinical data of dexibuprofen. Clin. Rheumatol. 2001, 20, S15–S21.
11) Kaehler, S.T.; Phleps, W.; Hesse, E. Dexibuprofen: Pharmacology, therapeutic uses and safety. Inflammopharmacology 2003, 11, 371–383.
12) Khalid, Q.; Ahmad, M.; Usman, M.; Batool, F.; Shamshad, N.; Rehman, M. Novel β -cyclodextrin nanosponges by chain growth condensation for solubility enhancement of dexibuprofen: Characterization and acute oral toxicity studies. J. Drug Deliv. Sci. Technol. 2021, 61, 102089.
13) Evans, A.M.; Nation, R.L.; Sansom, L.N.; Bochner, F.; Somogyi, A.A. Effect of racemic ibuprofen dose on the magnitude and duration of platelet cyclo-oxygenase inhibition: Relationship between inhibition of thromboxane production and the plasma unbound concentration of S (+)-ibuprofen. Br. J. Clin. Pharmacol. 1991, 31, 131–138.
14) Wsól, V.; Skálová, L.; Szotáková, B. Chiral inversion of drugs: Coincidence or principle? Curr. Drug Metab. 2004, 5, 517–533.
15) Lipinski C. Poor aqueous solubility–an industry wide problem in drug discovery. Am Pharm Rev. 2002;5(3):82–85.
16) Bittner B, Mountfield RJ. Formulations and related activities for the oral administration of poorly water-soluble compounds in early discovery animal studies: an overview of frequently applied approaches. Part 1. Drugs Made Ger. 2002;45(1):18–24.
17) Bittner B, Mountfield R. Intravenous administration of poorly soluble new drug entities in early drug discovery: the potential impact of formulation on pharmacokinetic parameters. Curr Opin Drug Discov Devel. 2002;5(1):59–71.
18) Modi A, Tayade P. Enhancement of dissolution profile by solid dispersion (kneading) technique. AAPS Pharm SciTech. 2006;7(3): E87–E92.
19) Sarker DK. Engineering of nanoemulsions for drug delivery. Curr Drug Deliv. 2005;2(4):297–310.
20) Jyothi NVN, Prasanna PM, Sakarkar SN, Prabha KS, Ramaiah PS, Srawan G. Microencapsulation techniques, factors influencing encapsulation efficiency. J Microencapsul. 2010;27(3):187–197.
21) Kedar U, Phutane P, Shidhaye S, Kadam V. Advances in polymeric micelles for drug delivery and tumor targeting. Nanomedicine. 2010;6(6): 714–729.
22) Serajuddin AT. Salt formation to improve drug solubility. Adv Drug Deliv Rev. 2007;59(7):603–616.