
Research Article



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**DEVELOPMENT AND CHARACTERIZATION OF NANO SUSPENSIONS
OF ACECLOFENAC SODIUM**

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Abstract

Aceclofenac is an anti-inflammatory and analgesic agent. For inflammatory conditions of eye a prolonged action pharmaceutical may be recommended. The present work aims to prepare a sustained release nanosuspension of aceclofenac using Eudragit RS 100 by quasi-emulsion solvent diffusion technique. The resulting nanosuspensions showed interesting mean sizes for ophthalmic applications. The particle size can be influenced by various process and parameters, such as drug concentration of stabilizers, cooling conditions, and homogenization procedure. Further it has shown that formulating aceclofenac as a nanosuspension is highly successful in sustained release of drug. Particle size was found using Atomic force microscope (AFM) and the average particle size was found to be 73.27 nm. In vitro drug release studies are carried out using dialysis membrane with 12,000 cut off value. The drug release studies was found to be decreasing with increase in the percentage of the drug polymer ratio. The formulation B2 with drug polymer ratio (2:3) was found to be having the higher retardation capacity.

Key words: Ibuprofen, Eudragit RS 100, Nanosuspension, Ophthalmic delivery.

Introduction

The inflammatory response of ocular tissues is a common side effect associated with ophthalmic surgery. It can interfere with the normal function of the eye, whose optic transparency must be maintained. Along with corticosteroids, non-steroidal anti-inflammatory drugs (NSAIDs) are used during eye surgery therapy. Surgical or mechanical traumas of the anterior segment of the eye cause a vascular inflammatory reaction due to the disruption of the blood–aqueous barrier,

with a marked rise in protein content of the aqueous humour, a transient ocular hypertension and miosis. Miosis is frequent problem during extracapsular cataract surgery despite the instillation of topical mydriatic agents. Aryl propionic type NSAID drugs, such as ibuprofen can antagonize the papillary constriction during intra ocular surgery by blocking cyclo oxygenase pathway and reducing polymorphonuclear leukocyte infiltration in the aqueous humour. Most ocular diseases are treated with topical application of

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drug solutions administered as eye drops; however they often require frequent instillation of highly concentrated solutions, due to rapid pre corneal loss from eye.

Materials and methods

Materials

Mumbai and benz-alkonium chloride from Rankem chemicals pvt. Ltd, New delhi Eudragit RS 100 purchased from Evonik Degussa india Pvt. Ltd, Aceclofenac from Madras pharmaceuticals Pvt. Ltd, Tween 80 Cisco research laboratories Pvt .Ltd.

Preparation of nano suspension

Eudragit RS 100 nanosuspensions were obtained in the presence or absence of aceclofenac, at different drug/polymer weight ratios and using different rates of agitation, using an adaptation of the quasi-emulsion solvent diffusion technique. The drug and

polymer were co-dissolved in ethanol at room temperature in ethanol(2ml).The solution was slowly injected (0.5 ml/ min), with a syringe containing thin Teflon tube, in to 50ml water containing Tween 80(0.02%, w/v), and benzalkonium chloride(0.15w/v),and kept at a low temperature in an iced water bath. During injection, the mixture was highly placed by an high speed homogenizer at different agitation. The solution immediately turned in to pseudo-emulsion of the drug and polymer ethanol solution in the external aqueous phase. The counter diffusion of ethanol and water out of and into the emulsion micro-droplets, respectively and the gradual evaporation of the organic solvent determined the in situ precipitation of the drug, with the formation of matrix-type nanoparticles. Ethanol residues were left to evaporate off under slow magnetic stirring of the nanosuspensions at room temperature for 8-12hr.

Table No. 01: Formulative variables of aceclofenac loaded eudragit L100 nanosuspensions. Stirring speed was 20,500 RPM, 13,500 RPM, 9,500 RPM, for batches A, B and C respectively.

S.No	Formulation	Drug (mg)	Polymer (mg)	Agitation speed (rpm)
1.	A1	50	50	20 500
2.	A2	33	67	20 500
3.	A3	10	90	20 500
4.	B1	50	50	13 500
5.	B2	33	67	13 500
6.	B3	10	90	13 500
7.	C1	50	50	9500
8.	C2	33	67	9500
9.	C3	10	90	9500

Results and discussion

Average particle size and amount of unincorporated drug

Aceclofenac loaded nanoparticles using different preparative variables are obtained: the drug to polymer weight ratio (50,33,10) , the total amount of drug and polymer ratio in the initial ethanol solution (100mg) and the

agitation speed (from 9500 to 20 500) during the formulation of nanosuspension. Such variables could influence the particle size and the drug release from them. Average particle size measured after preparation of the nanosuspension. The unincorporated drug is measured by uv-analysis at λ_{max} 275nm.

Table No. 02: Average particle size values and amount of an incorporated drug

S.No	Formulation	Particle size(nm)	% Drug entrapment
1.	A1	37.6	83.3
2.	A2	43.2	90
3.	A3	72.5	95.7
4.	B1	90.96	77.7
5.	B2	74.80	95.16
6.	B3	77.80	95.2
7.	C1	90.23	96.6
8.	C2	110.23	95.75
9.	C3	109.2	96.65

Invitro drug realease studies

Aceclofenac release from nanosuspensions was evaluated in triplicate over 3h by a dialysis system consisting of a spectrapormmemberane(cut-off:1200Da), loaded with 5 ml of nanosuspensions and soaked in a

0.14M phosphate buffer solution(pH7.4), at room temperature and under slow magnetic stirring. At regular time intervals 1ml aliquots of the external medium were withdrawn and immediately replaced with the same volume of fresh buffer.

Table No. 03: Invitro drug release studies

S.No	Time(min)	Percentage of drug release								
		A1	A2	A3	B1	B2	B3	C1	C2	C3
1.	0	0	0	0	0	0	0	0	0	0
2.	30	77.6	33.9	18	68	11.8	15.1	36	15	21.5
3.	60	86.9	42.7	18.3	82.8	12	19.5	36.4	15.2	32.3
4.	90	101.7	51.5	27.3	115	27.2	30	63.8	27.8	38
5.	120	105.7	69.3	33.9	-	35.2	34.3	92.4	44.2	46.2
6.	150	-	71.4	42.8	-	41.5	42.8	116	51.2	44.2

Stability studies of the formulations

The physical stability of the nanosuspensions was evaluated after storage for 6 months under different temperature conditions. Exact volumes of each nanosuspension were stored and placed at either room temperature or 4–6 8C (re-frigerator) away from direct light. Aliquots of 500 ml were withdrawn every month to determine particle size.

Conclusion

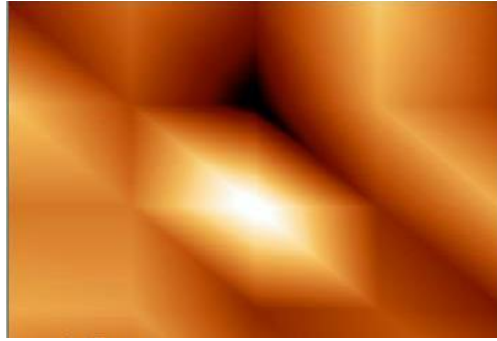
The aim is to prepare aceclofenac nano - suspensions using Eudragit RS 100. The nanosuspensions prepared by quasi emulsion solvent diffusion technique. They are obtained using drug (50,33,10) polymer(50,67,90) ratio at different agitation speed. The evaluation

parameters like percentage of drug entrapment, particle size, invitro drug release studies were performed. In drug entrapment studies, all the formulations was found to have more than 80%entrapment (83.7%-96.6%). Particle size was found using Atomic force microscope (AFM) and the average particle size was found to be73.27 nm. The particle size is in range of (37.36-110.8). Invitro drug release studies are carried out using dialysis membrane with 12,000 cut off value. The drug release studies were found to be decreasing with increase in the percentage of the drug polymer ratio. The formulation B2with drug polymer ratio (2:3) was found to be having thee higher retardation capacity.

A1-37.2nm



A2-43.2nm



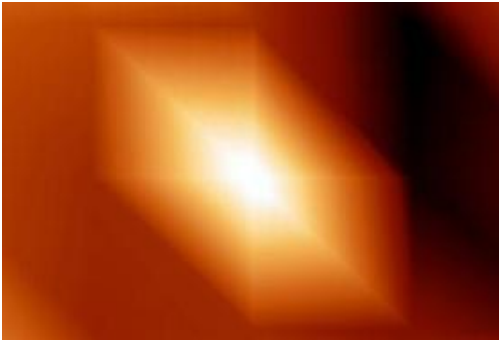
A3-72.5 nm



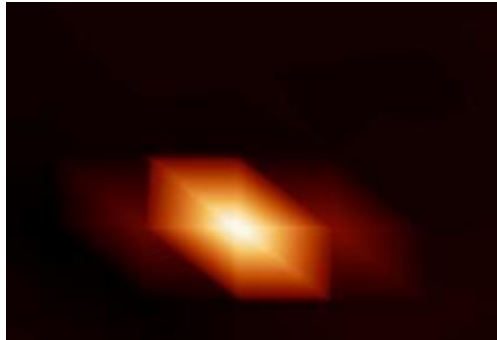
B1-90.96nm



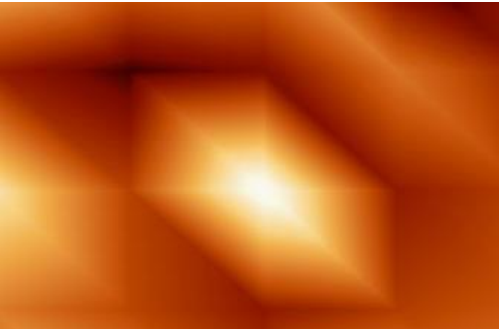
B2-74.80nm



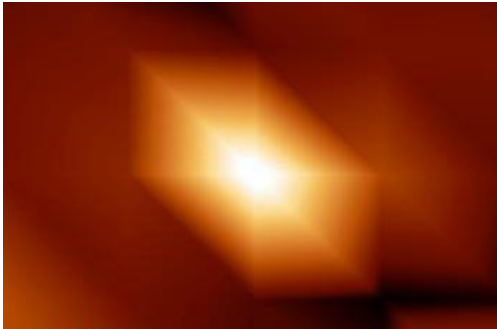
B3-77.80nm



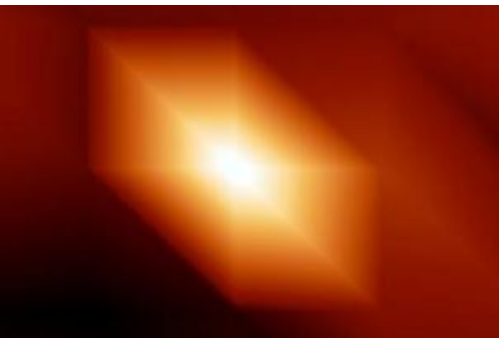
C1-90.23nm



C2-110.23nm



C3-109.2



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