Research Article
CODEN (USA): IJPLCP

[Dhakad *et al.*, 3(6): June, 2012]
ISSN: 0976-7126

INTERNATIONAL JOURNAL OF PHARMACY & LIFE SCIENCES

Development and evaluation of floating pulsatile multiparticulate drug delivery system using aceclofenac as a model drug

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Abstract

Development and evaluation of floating, pulsatile, multiparticulate drug delivery system using aceclofenac as a model drug. Pulsatile drug delivery systems are gaining importance as these systems deliver the drug at specific time as per the pathophysiological need of the disease, resulting in improved patient therapeutic efficacy and compliance. Diseases wherein PDDS are promising include asthma, peptic ulcer, cardiovascular diseases, arthritis, attention deficit syndrome in children, and hypercholesterolemia. Dispersion technique was used for the preparation of beads of aceclofenac by using polymer of low methoxylated pectin, sodium alginate and gellan gum and combination of them. The active component was characterized using modern techniques like UV, IR, and DSC etc. The present study is aimed to develop floating, pulsatile, multiparticulate drug delivery system intended for chronopharmacotherapy in arthritis. Cross-linked beads were prepared by using low methoxylated pectin, sodium alginate, low methoxylated pectin + Sodium alginate and low methoxylated pectin + deacetylated gellan by acid-base reaction during ionotropic gelation. Beads were dried in oven at 500 ºC for 4hr. Aceclofenac was used as a model drug for encapsulation. Drug loaded multiparticulates were subjected to various characterization and evaluation parameters like entrapment efficiency, buoyancy study, surface topography.From the above evaluation studies, low methoxylated beads contain high entrapment efficiency with about 90% drug release. This optimized batch (F6) was kept for stability studies at 40°C ± 5°C and 75% RH ± 5% RH for 30 days in order to know the influence of temperature and relative humidity on drug content and drug release profile.

Key-Words: DDS, Aceclofenac, Evaluation

Introduction

With the advancement of the technologies in the pharmaceutical field, drug delivery systems have drawn an increasing interest over the last few decades. Nowadays, the emphasis of pharmaceutical galenic research is turned towards the development of more efficacious drug delivery systems with already existing molecule rather going for new drug discovery because of the inherent hurdles posed in drug discovery and development process [1]. Traditionally, drug delivery has meant for getting a simple chemical absorbed predictably from the gut or from the site of injection. A second-generation drug delivery goal has been the perfection of continuous, constant rate delivery of bioactive agents. However, living organisms require different amounts of drug at predictably different times within the circadian cycle which will maximize desired and minimize undesired drug effects[2].

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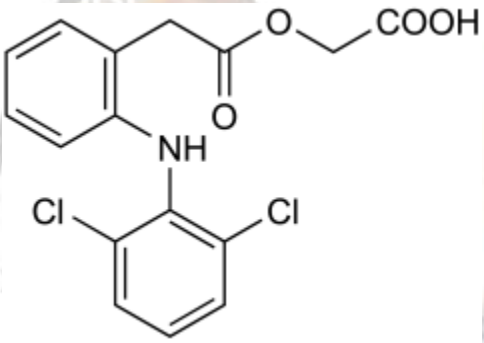
Till early nineties efforts have been made to design the drug delivery system which will release the drug fairly at constant rate. In fact these systems turned to be one of the most successful systems in delivering the drug molecule [3]. But still for many of the drugs, use of such systems is not suitable because of a number of reasons. This is particularly true in cases where the drug is subjected to large metabolic degradation. Due to 'first pass effect' there will be reduction in the bioavailability of the drug because; gradual release can result in greater degradation. Secondly drugs with short half-life need to be administered repeatedly which results in patient non-compliance. Further, in case of chronic treatment, where the drug is given in sustained release dosage form, continuous exposure of the drug to body may lead to adverse effect. For example, diabetes mellitus requires chronic treatment with sustained release formulations of drugs like sulfonylurea which will damage the pancreas earlier than the corresponding immediate release dosage form. Lastly, drugs which exhibit tolerance should not be delivered at a constant rate, since the drug effect decreases with time at constant drug level. In addition drug toxicity increases with time when drug levels are

held constant. In such cases it is preferable to develop a dosage form which will provide desired concentration of drug at particular time point only [4].

Nowadays, concept of chronopharmaceutics has emerged, wherein, research is devoted to the design and evaluation of drug delivery systems that release a therapeutic agent at a rhythm that ideally matches the biological requirement of a given disease therapy. Diseases where a constant drug levels are not preferred, but needs a pulse of therapeutic concentration in a periodic manner acts as a push for the development of "Pulsatile Drug Delivery Systems[5]".

Aceclofenac: Structure



IUPAC Name: 2-[(2, 6- Dichlorophenyl amino) phenyl] acetoxyacetic acid.

Molecular Formula: $C_{16}H_{13}Cl_2NO_4$

Molecular weight: 354.19 g/mol.

Melting Range: 149-150 ^{0}C

Description: A white to almost white crystalline powder. It is practically insoluble in water, soluble in alcohol and methyl alcohol: freely soluble in acetone and dimethylformamide.

Half-Life: Elimination half life is approximately 4hrs.

Volume of distribution: Apparent volume of distribution is approx 25 L.

Dose: An usual dose of 100mg. twice daily is administered with a reduction to 100 mg daily for patients with hepatic impairment.

Material and Methods

Collection of Plant material (Specimens)

Drugs: Aceclofenac BP (Suyash lab. Ltd.Maharastra),

Excipients: Low Methoxylated Pectin(C.P.Kelco lab Denmark) , Gellan Gum (Deacetylated) { C.P.Kelco lab Denmark}, Sodium Alginate{ Hi Media lab.Pvt.Ltd Mumbai}.

Methodology for Aceclofenac

Analysis of Aceclofenac:

Calibration curve of aceclofenac in acidic buffer (pH 1.2): Various drug concentrations (5-35µg/ml) in acidic buffer (pH 1.2) were prepared and the absorbance was measured at 273nm (Shimadzu 1700). For the standard graph, 10mg of aceclofenac was accurately weighed and dissolved in a mixture of 50 ml methanol and 50 ml acidic buffer (pH 1.2). Then 0.5ml, 1ml, 1.5ml, 2ml, 2.5ml, 3ml and 3.5ml of this solution was further diluted to 10ml with acidic buffer (pH 1.2) and the absorbance was taken at 273 nm using UV spectrophotometer (Shimadzu 1700). [fig. no 1]

Calibration curve of aceclofenac in phosphate buffer (pH 6.8): Various drug concentrations (5-30µg/ml) in phosphate buffer (pH 6.8) were prepared and the absorbance was measured at 275nm. For the standard graph, 10mg of aceclofenac was accurately weighed and dissolved in 100ml of phosphate buffer (pH 6.8). Then 0.5ml, 1ml, 1.5ml, 2ml, 2.5ml, 3ml of this solution was further diluted to 10ml with phosphate buffer (pH 6.8) and the absorbance was taken at 275 nm using UV spectrophotometer (Shimadzu 1700). [fig. no.2]

Calibration curve of aceclofenac in phosphate buffer (pH 7.4): Various drug concentrations (5-30µg/ml) in phosphate buffer (pH 7.4) were prepared and the absorbance was measured at 275nm. For the standard graph, 10mg of aceclofenac was accurately weighed and dissolved in 100ml of phosphate buffer (pH 6.8). Then 0.5ml, 1ml, 1.5ml, 2ml, 2.5ml and 3ml of this solution was further diluted to 10ml with phosphate buffer (pH 7.4) and the absorbance was taken at 275 nm using UV spectrophotometer (Shimadzu 1700). [fig no.3]

Preparation of beads [6,7]

Preparation of pectin beads: In this present work solution of pectin prepared by dissolving 300 mg of polymer in a warmed 10ml deionised water. On complete solution, an accurately weighed quantity of 100mg of Aceclofenac and different concentration of sodium bicarbonate ($NaHCO_3$) were added in increments as given in table12. This dispersion was sonicated for 30 min to remove any air bubbles that have been formed during stirring process (Ultrasonicator, Lab hosp). This dispersion was dropped through 23# needle in to 50 ml calcium chloride ($CaCl_2$) solution containing 8 ml of 10% acetic acid.

Preparation of sodium alginate beads: Then the optimized sodium bicarbonate concentration (100mg) was kept same for sodium alginate with different concentration of polymers as given in table13 then this dispersion was dropped via 23# needle in to 50ml calcium chloride ($CaCl_2$) solution containing 8ml of 10% acetic acid.

Preparation of combined sodium alginate and pectin beads [8] :Combined sodium alginate beads along with pectin were prepared with same concentration of

sodium bicarbonate (100mg) with different concentration of polymer, then this dispersion was dropped via 23# needle in to 50ml calcium chloride ($CaCl_2$) solution containing 8ml of 10 % acetic acid.

Preparation of combined deacetylated gellan and pectin beads: Combined deacetylated gellan along with pectin beads, were prepared with same concentration of sodium bicarbonate (100mg) with different concentration of polymer, then this dispersion was dropped via 23# needle in to 50ml calcium chloride ($CaCl_2$) solution containing 8ml of 10% acetic acid.

The droplets of each dispersion were instaneously gelled into discrete Aceclofenac-pectin, Aceclofenac-Sodium alginate, Aceclofenac- Sodium alginate pectin beads and Aceclofenac-pectin gellan. The calcium-pectin, calcium-sodium alginate, calcium pectin-sodium alginate and calcium pectin gellan matrices were further stirred for 15 min. Then the beads were allowed to cure in $CaCl_2$ solution. The beads were then filtered, washed with distilled water and oven dried at 50^0 C for 4hrs.

Results and Discussion

Calibration curve of aceclofenac in acidic buffer (pH 1.2): The calibration curve for Aceclofenac in acidic buffer (pH 1.2) is in the concentration range of 5-35 µg /ml

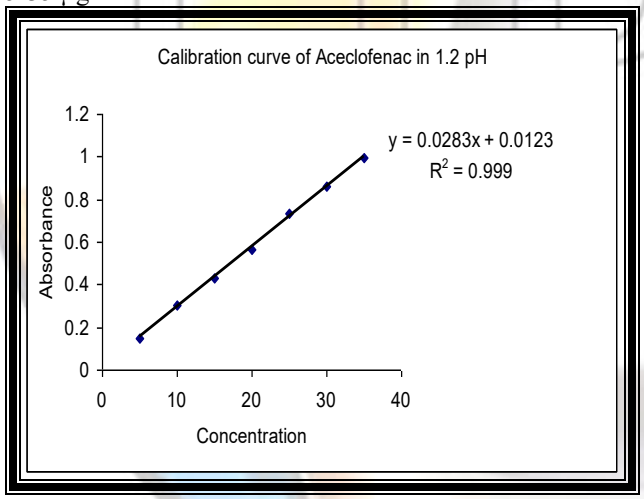


Fig.1: Calibration curve of Aceclofenac in acidic buffer pH 1.2

Correlation Coefficient (R^2) = 0.999
Equation for regressed line; Y= 0.0283x + 0.0123
Where X= value for concentration
Y= Value for absorbance
0.0283 = slope of regressed line

Calibration curve of Aceclofenac in basic buffer (pH 6.8)

The calibration curve for Aceclofenac in phosphate buffer (pH 6.8) is in the concentration range of 5-30 µg /ml.

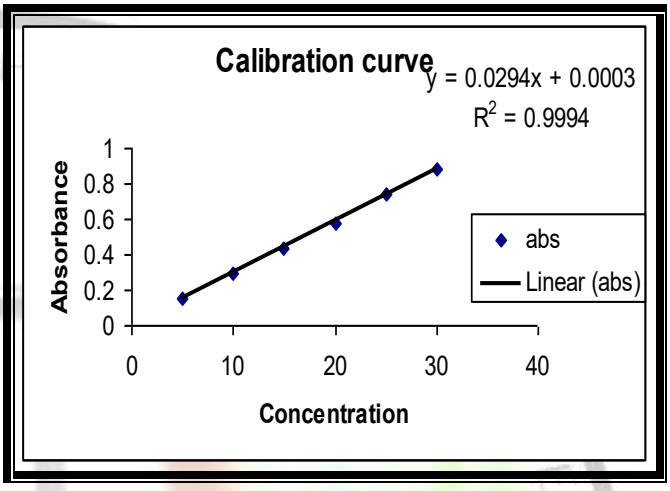


Fig.2: Calibration curve of Aceclofenac in phosphate buffer pH (6.8)

Correlation Coefficient (R^2) = 0.9994
Equation for regressed line; Y= 0.0294x + 0.0003
Where X= value for concentration
Y= value for absorbance
0.0294 = slope of regressed line

Calibration curve of Aceclofenac in phosphate buffer (pH 7.4)

The calibration curve for Aceclofenac in phosphate buffer (pH 7.4) is in the concentration range of 5-30 µg /ml.

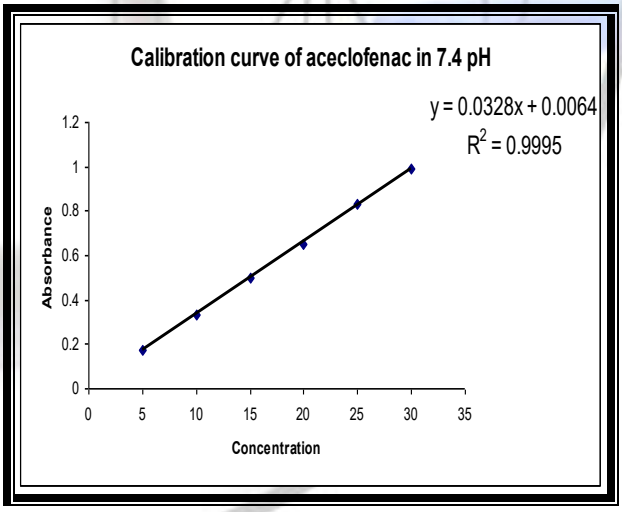


Fig.3: Calibration curve of Aceclofenac in phosphate buffer pH 7.4

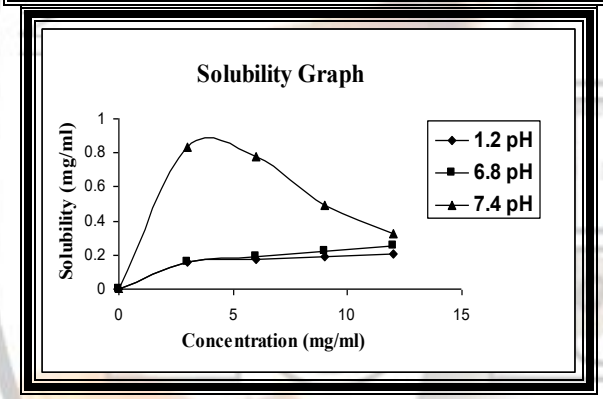
Correlation Coefficient (R^2) = 0.9995
Equation for regressed line; Y= 0.0328x + 0.0064
Where X= value for concentration

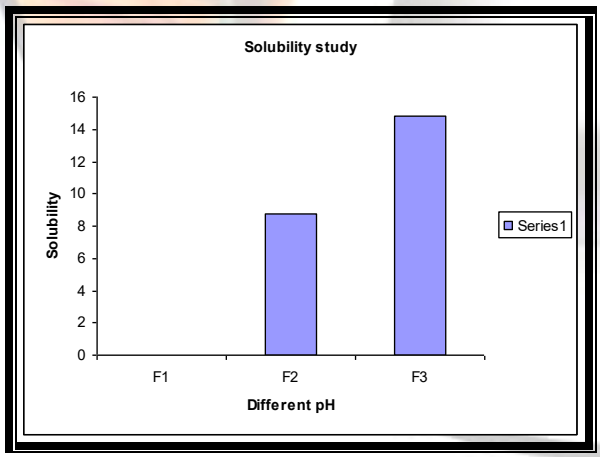
Y= regressed value of absorbance
0.0328 = slope of regressed line

Preformulation study

Solubility study: The solubility of aceclofenac in different pH condition was checked which is given in following table no.1:

Concentration (mg/ml)	Solubility (mg/ml)		
	1.2 pH	6.8 pH	7.4 pH
3	0.0052898	3.391156	2.531024
6	0.0059258	6.520408	11.82681
9	0.0064205	7.540816	14.85843
12	0.0069859	8.731293	10.94277





F1 = 1.2 pH, F2 = 6.8 pH, F3 = 7.4 pH

Fourier Transform Infra Red Spectroscopy

Infra red spectra of Aceclofenac and physical mixture of all polymers have shown in fig 4, 5, 6, 7, 8, and table 2. From this it is observed that there is no interaction between drug and polymer.

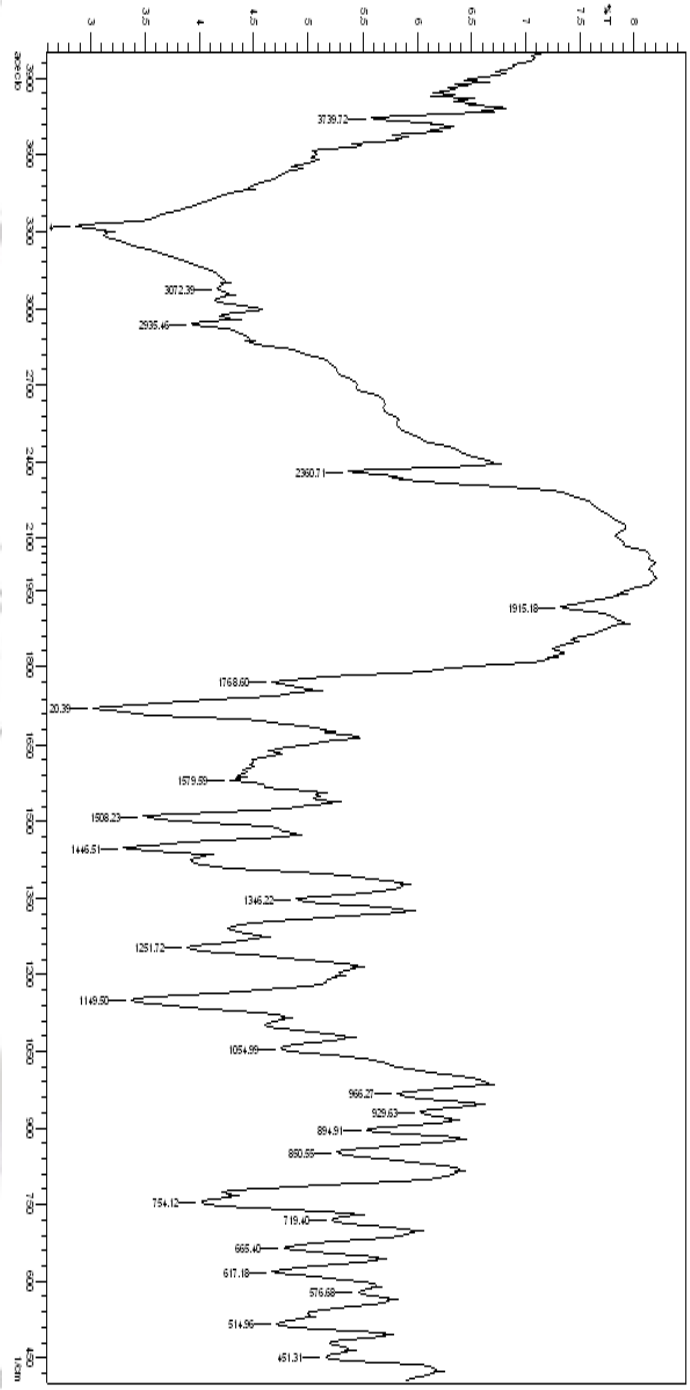


Fig 4: IR spectra of Aceclofenac

Table 2: IR peaks showing drug interaction

Polymers	Drug peak	Drug+polymer peak	Interaction
LM104AS	717.54,1504.53 1716.7,1093.67, 3028.34	717.54,1504.53 1716.7,1068.7, 3025.5	No
Sodium alginate	717.54,1504.53 1716.7,1093.67, 3028.34	717.54,1504.53 1716.7,1068.7, 3025.5	No
Sodium alginate + LM104AS	717.54,1504.53 1716.7,1093.67, 3028.34	717.54,1504.53 1716.7,1068.7, 3025.5	No

Optimization of acetic acid

Table 3 shows the concentration of acetic acid in $CaCl_2$ solution. From this it is observed that at 2 ml and 4 ml concentration of10% acetic acid in $CaCl_2$ solution it does not show buoyancy to the formulation. At 6 ml and 8 ml concentration of 10% acetic acid in $CaCl_2$ solution beads show good floating property but at 6 ml the beads show lag time. At 10 ml concentration of 10% acetic acid in $CaCl_2$ solution beads show bursting during formulation. Therefore 8 ml concentration of acetic acid is used for further studies.

Table 3: Effect of acetic acid concentration on floating ability of beads.

Polymer	Acetic acid concentration in ml				
LM104AS	2	4	6	8	10
S.A	2	4	6	8	10
S.A + LM104AS	2	4	6	8	10
D.G + LM 104 AS	2	4	6	8	10

Selection of effervescent agent

Table 4 shows different effervescent agents. From this it is observed that the beads containing K_2CO_3 and Na_2CO_3, could not be produced as a viscous gel formed before extrusion through the needle. The beads containing $CaCO_3$, exhibited poor floating ability and beads start sinking after 5hrs. Therefore $NaHCO_3$, is used as effervescent agent for further batches.

Table 4: Effect of different effervescent agents on floating property of beads

Effervescent agents	Concentration
$NaHCO_3$	20%
$CaCO_3$	20%
K_2CO_3	20%
Na_2CO_3	20%

Effect of $CaCl_2$ concentration on drug entrapment

The effect of Calcium chloride concentration on entrapment efficiency of the calcium pectinate beads is depicted in table 5. When the calcium chloride concentration increases, entrapment efficiency decreases. This is due to increasing concentration of calcium chloride leads to greater degree of cross-linking and aggregation of the initial dimmers giving higher gel strength.

Table 5: Effect of $CaCl_2$ concentration on entrapment efficiency of beads

% of $CaCl_2$	% Drug Entrapment
2	65
3	60
4	55
5	48

Preparation of beads

Calcium alginate, calcium pectinate, calcium alginate pectinate and calcium pectinate gellan are beneficial matrices as they offers a simple, multiparticulte, pulsatile drug delivery system for drugs because of it's highly pH dependent characteristics. As these beads show minimum swelling with minimum drug release in acidic media and maximum swelling with maximum drug release in basic media. Table 6, 7, 8, 9 and 10 show formula for calcium pectinate, calcium alginate, calcium alginate pectinate and calcium pectinate gellan. Firstly sodium bicarbonate concentration was optimized by using LM104AS as a polymer. It was observed that beads formulated with higher amount of sodium bicarbonate (F1 to F3) shows bursting during formulation. Beads obtained from batch F4 containing 150 mg does not have proper shape and batch F5 and F6 containing 125 mg and 100 mg of sodium bicarbonate respectively have proper integrity. Therefore sodium bicarbonate concentration (100mg) was used for further polymers (sodium alginate,

sodium alginate along with LM104AS and gellan along with LM104AS). Preliminary study was carried out using different concentration of polymers. It was observed that when sodium alginate was used in 3% (w/v) concentration produces fragile beads. For sodium alginate along with the LM104AS concentration of polymer (2% w/v and 1% w/v and vice versa) produces fragile beads and does not have proper shape. Beads containing deacetylated gellan concentration (2% w/v) and (1%w/v) could not be produced as, a viscous gel formed before extrusion through the needle and at (0.4% w/v) and 0.6% w/v) concentration of deacetylated gellan beads are formed but, it does not have proper consistency. Therefore deacetylated gellan and LM104AS combination is used. Hence, from the above study the concentration of pectin (3%w/v), sodium alginate (3.25%w/v), sodium alginate along with low methoxylated pectin (1.5%w/v level of each) and low methoxylated pectin along with deacetylated gellan (2.4%w/v, 0.4% w/v levels respectively) is used in F6, F8, F11 and F16 respectively. Therefore batches F6, F8, F11 and F16 were used for further characterization of the beads. The solution of these polymers containing 100mg of drug, 100 mg of $NaHCO_3$ dropped in $CaCl_2$ solution shows excellent floating ability.

Table 6: Composition for the formulation of the beads with drug and pectin

BATCHES	F1	F2	F3	F4	F5	F6
Drug (mg)	100	100	100	100	100	100
$NaHCO_3$(mg)	250	225	200	150	125	100
Acetic acid (ml)	8	8	8	8	8	8
LM104AS (mg)	300	300	300	300	300	300
$CaCl_2$ (w/v)	2%	2%	2%	2%	2%	2%

Table 7: Composition for the formulation of the beads with drug and Sodium alginate

Batches	F7	F8
Drug (mg)	100	100
$NaHCO_3$ (mg)	100	100
Acetic acid (ml)	8	8
Sodium alginate (mg)	300	325
$CaCl_2$ (w/v)	2%	2%

Table 8: Composition for the formulation of the beads with drug, Sodium alginate and pectin

batches	F9	F10	F11
Drug (mg)	100	100	100
$NaHCO_3$ (mg)	100	100	100
Acetic acid (ml)	8	8	8
Sodium alginate+ LM104AS (mg)	200+100	100+200	150+150
$CaCl_2$ (w/v)	2%	2%	2%

Table 9: Composition for the formulation of the beads with drug and Gellan

BATCHES	F12	F13	F14	F15
Drug (mg)	100	100	100	100
$NaHCO_3$ (mg)	100	100	100	100
Acetic acid (ml)	8	8	8	8
Gellan(mg)	200	100	60	40
$CaCl_2$(w/v)	2%	2%	2%	2%

Table 10: Composition for the formulation of the beads with drug, pectin and Gellan gum

BATCH	F1
Drug (mg)	100
$NaHCO_3$ (mg)	100
Acetic acid (ml)	8
Gellan (mg)	40
LM104AS (mg)	240
$CaCl_2$(w/v)	2%

Yield of production

The production yield of beads prepared by ionic gelation technique varied with different polymers as it was observed that production yields of Sodium alginate is > low methoxylated pectin + sodium alginate > low methoxylated pectin> low methoxylated pectin + deacetylated gellan. Yields of production for the batches F6, F8, F11 and F16 are depicted in table 11.

Determination of drug entrapment capacity

Drug entrapment efficiency for the batches F6, F8, F11 and F16 is depicted in table 11. Batch prepared with low methoxylated pectin LM104AS shows greater entrapment. The maximum entrapment capacity is in order of LM104AS> Sodium alginate + LM104AS> Sodium alginate > low methoxylated pectin+ deacetylated gellan. The increased entrapment efficiciency in LM104AS is due to high and quick gelling ability in $CaCl_2$ solution, Sodium alginate is having lower entrapment due to low viscosity. Drug entrapment depends on various factors like physico-chemical property of drug, polymer and the amount of cross linking agent.

Size analysis

Sizes of beads (F6, F8, F11 and F16) which are taken by digital photomicroscope with the help of digital camera are depicted ion table 11.

Table 11: Yield of production & drug entrapment efficiency

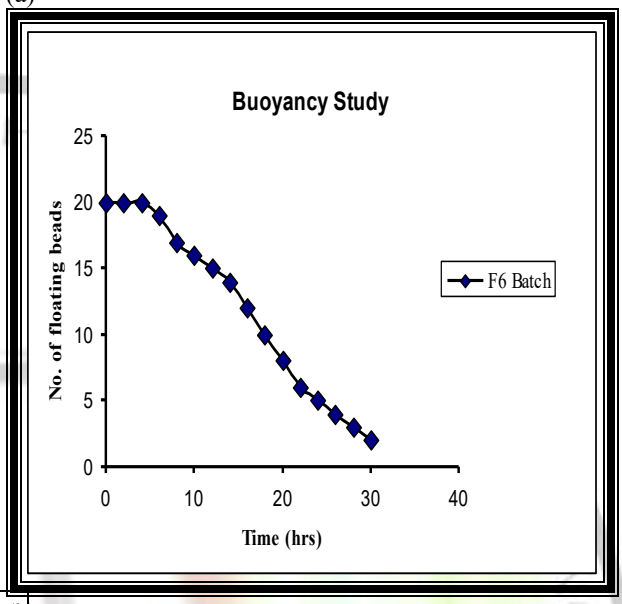
Polymers	Yield of production (%)	Drug entrapment efficiency (%)	Size (µM)
LM104AS (F6)	90.40±0.75	65.45±0.76	922.66±0.57
Sodium alginate (F8)	93.36±1.13	50.49±0.75	854±1
Sodium alginate + LM104AS (F11)	92.5±0.77	55.06±0.88	810.33±1.52
LM104AS+ Deacetylated gellan (F16)	87.46±0.85	50.41±1.23	1310±0.69

Data were presented as mean ± SD of triplicate experiments.

Buoyancy Study

Floating property of the beads containing optimized concentration of sodium bicarbonate (F6) in 1.2 pH buffer was studied by visual observation. Time required for sinking of the beads was observed. All the beads show good floating without any lag time. All the beads remained floating for about 5 hrs. Total time required for all the beads for sinking is about 30 hrs. Floating property of the beads is due to low density and porous nature of the beads. From this it is observed that the beads show excellent floating capacity. Buoyancy study of the sample is shown in figure 9.

(a)



(b)

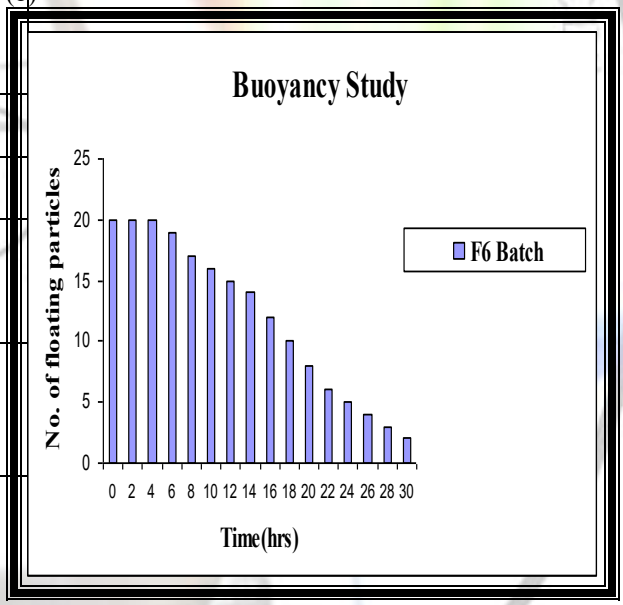


Fig: 9 (a) Graph for buoyancy study of F6 batch showing 5 hrs floating of the beads (b) Columns for buoyancy F6 batch showing 5hrs floating of the beads.

Swelling Study: Swelling study of the beads (batches F6, F8, F11 and F16) is depicted in table 12. As calcium alginate, calcium pectinate, calcium alginate pectinate and calcium pectinate gellan beads show maximum swelling in basic buffer i.e.pH 7.4 than acidic buffer. The beads show excellent swelling and bursting in the basic buffer.

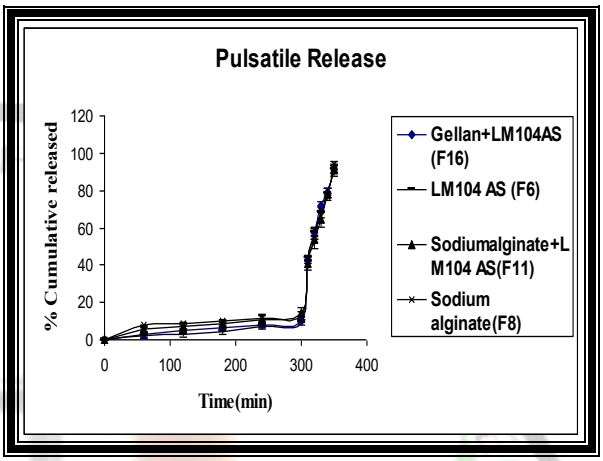
Table 12: Swelling study of F6, F8, F11 and F16 formulation in acidic and basic media

Polymers	Swelling study in acidic media	Swelling study in basic media
LM104AS (F6)	8.51	702.32
Sodium alginate (F8)	8.69	759.09
Sodium alginate+ LM104AS (F11)	10.63	686.95
LM104AS+ Deacetylated gellan (F16)	8.75	659.48

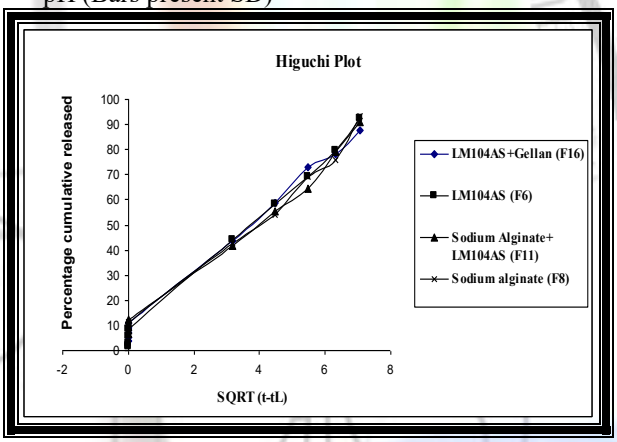
***In Vitro* study:** The cumulative release of the beads batches (F6, F8, F11 and F16) is depicted in table 13 and fig 10 (a) was found to be 90-94%. All the batches (F6, F8, F11 and F16) of the beads show about 5-12% of drug release in acidic media. Drug release in acidic media depends on the swelling capacity of the polymer. Pectin gives minimum swelling than other polymer with minimum drug release about 5% in acidic media. All the polymers like calcium alginate, calcium pectinate, calcium alginate pectinate and calcium pectinate gellan shows rapid swelling and gel relaxation in 7.4 pH and showing bursting of beads with drug release in the range of 90-94% in alkaline pH. The aceclofenac is freely soluble in 7.4 pH that resulted in rapid and complete drug release in 7.4 pH. Hence the porous beads show lag time in acidic media due to low solubility of drug and polymer and then immediate pulse release in alkaline media.

Table 13: Dissolution study of F6, F8, F11 and F16 batches

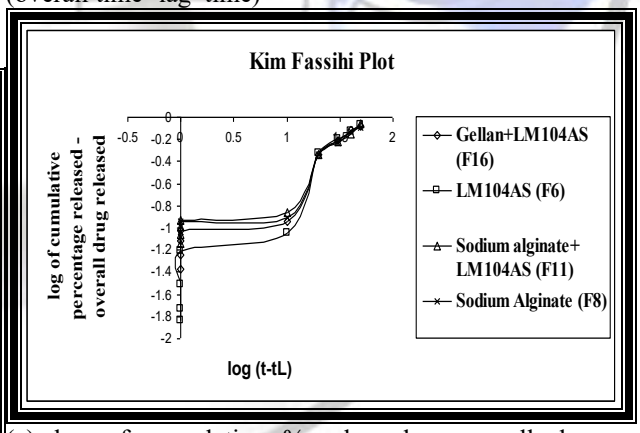
Time (Min)	LM104AS (F6)	Sodium Alginate (F8)	LM104AS + S.A (F11)	Gellan (Deacetylated) + LM104AS (F16)
60	1.3285	7.8042	6.5321	3.6063
120	1.7032	8.6108	7.9677	5.4073
180	2.8147	9.6125	9.4110	7.1981
240	5.7078	10.5558	10.7986	8.9889
300	8.3108	11.4405	12.5115	10.7797
310	44.1729	42.7967	41.5680	43.5106
320	58.4993	54.0534	55.2669	58.9985
330	69.0652	69.1856	64.2834	72.9998
340	79.8533	75.6880	79.3300	77.9751
350	92.5286	93.2448	90.7848	87.7982



(a) *In Vitro* release profile in 1.2 pH for 5 hrs and then pulse in 7.4 pH (Bars present SD)



(b) Aceclofenac % cumulative release vs. square root (overall time- lag time)



(c) log of cumulative % released – overall drug released vs. log (overall time- lag time)

Fig 10: Dissolution graph (a) Zero order (b) Higuchi plot (c) Kim and Fassihi plot

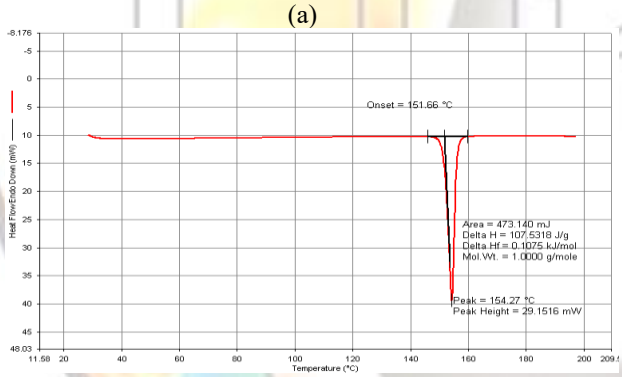
Table 14: Curve fitting data showing the mechanism of drug release

Polymer	Higuchi	Kim Fassihi	Kim Fassihi Equation (n values)
Lm104AS (F6)	0.996	0.9111	0.8974
Sodium alginate (F8)	0.992	0.8775	0.5171
Lm104AS + Sodium alginate (F11)	0.9921	0.896	0.5336
LM104AS+ Deacetylated gellan (F16)	0.996	0.8982	0.6428

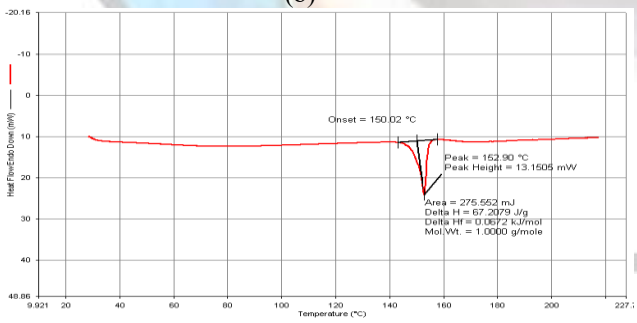
Differential scanning calorimetry

DSC thermograms of Aceclofenac, Aceclofenac and low methoxylated pectin and Aceclofenac loaded beads (F6) are shown in Fig 11 (a, b, c) and 12. Endothermic peaks were observed at 149-155 ^{0}C due to melting of drug and at 185-200^{0}C due to melting of polymer (low methoxylated pectin). In Aceclofenac loaded beads, Aceclofenac and low methoxylated pectin displayed their characteristic individual melting trends without any appreciable deviation.

(a)



(b)



(c)

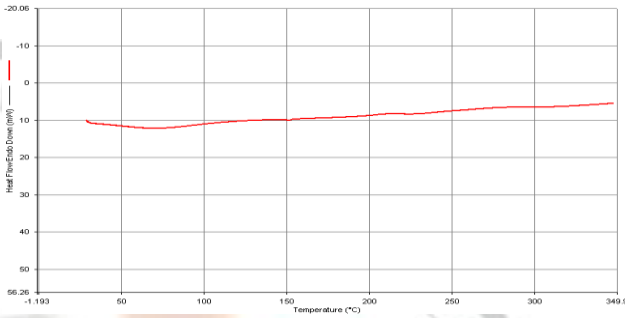


Fig 11: DSC thermograms of (a) Drug (b)Drug and polymer (c) beads (batchF6)

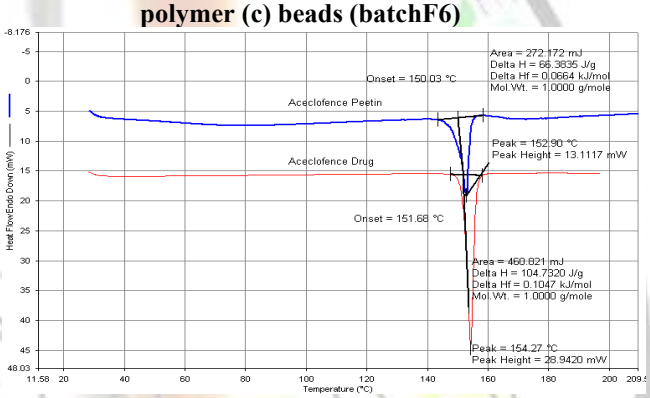


Fig 12: DSC overlay thermogram of (A) Drug (B) Polymer and drug

Pulsatile drug delivery system is the time and site specific drug delivery system, where there is rapid and transient release of certain amount of drug within a short time period immediately after predetermined off-release period. This will result in decreasing dosing frequency, increasing patient compliance, avoiding side effects of the drug due to continuous exposure of the drug in controlled release system and this system is advantageous for the drug which exhibit tolerance due to drug release at constant rate. More reliable gastric emptying patterns are observed for multiparticulate formulations as compared with single unit formulations, which suffer from “all or none concepts”.

The present study is aimed to develop floating, pulsatile, multiparticulate drug delivery system intended for chronopharmacotherapy in arthritis. Cross-linked beads were prepared by using low methoxylated pectin (LM104AS), sodium alginate, low methoxylated pectin (LM104AS) + Sodium alginate and low methoxylated pectin (LM104AS) + Deacetylated gellan by acid- base reaction during ionotropic gelation. Beads were dried in oven at 500 C for 4hr. Aceclofenac was used as a model drug for

encapsulation. Drug loaded multiparticulates were subjected to various characterization and evaluation parameters like entrapment efficiency, buoyancy study, surface topography.

From the above evaluation studies, low methoxylated beads contain high entrapment efficiency with about 90% drug release. This optimized batch (F6) was kept for stability studies at 40°C ± 5°C and 75% RH ± 5% RH for 30 days in order to know the influence of temperature and relative humidity on drug content and drug release profile.

References

1. Davis S.S., Illum L., 1998. "Drug delivery systems for challenging Molecule , *Int. J. Pharm,* 176, 1-8
2. Bi-Botti C., Youan, 2004. Chronopharmaceutics: gimmick or clinically relevant approach to drug delivery, *J. Control. Rel.* 98, 337-353.
3. Maroni, A., Zema. L., Cerea, M., 2005. Oral pulsatile drug delivery systems, *Expt. Opinion Drug Deli.,* 2, 855-871.
4. Pozzi F., Furlani P., Gazzaniga A., Davis S., 1994. The time clock system: a new oral dosage form for fast and complete release of drug after predetermined lag time, *J. Control. Rel.,* 31, 99-108.
5. Siegel R.A., Pitt C.G., 1995. A strategy for oscillatory drug release General scheme and simplified theory, *J. Control. Rel.*, 33, 173-188.
6. Choi B.Y., Park H.J., Hwang S.J. Park J.B., 2002. Preparation of alginate beads for floating drug delivery system: effects of CO_2 gas-forming agents. *Int. J. pharma.* 239, 81–91
7. Badve S., Sher P., Korde A. Pawar A., 2006. Development of hollow/porous calcium pectinate beads for floating-pulsatile drug delivery. *Eur. J. Pharma and Biopharma*. 65, 85-93.
8. Pillay V., Fassihi R., 1998. In vitro release modulation from cross linked pellets for site-specific drug delivery to the gastrointestinal tract I. Comparison of pH-responsive drug release and associated kinetics. *J. Control. Rel.* 59, 229-242.