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Formulation and Evaluation of Chitosan Based Tablets Dosage Forms

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ABSTRACT: The aim this study was to control the release profile of matrix tablets of Aceclofenac sodium prepared by using different concentrations of chitosan and microcrystalline cellulose as cross-linking agent with combination of various release retardant polymers. Matrix tablets were prepared by wet granulation technique. The granulesweresubjectedtoprecompression parameterssuchasangleofrepose, loosebulk density, tapped bulk density, compressibility index. Tablets were evaluated for weight variation,hardness,drugcontent,in-vitrodissolution,stabilitystudies,respectively.Drug-polymer compatibilitystudieswere determined byFTIRspectroscopy. Thegranulesofall formulationsexhibitedgoodflowandcompressibility. Itwasfoundthat gooddissolutionprofiletocontrolthedrugrelease.The drugrelease follows zero-order kinetics and the mechanism was found to be diffusion controlled and transport. FT-IR spectroscopic studies revealed no interaction between drug and polymer.Thecombinationofdifferent classesofpolymersanacceptablereleaseprofile canbe obtained in the fluctuating in vivo environment.

Keywords:Chitosan,controlledreleasematrixtablets, Aceclofenac,Polymer,FT-IR, Wet granulation

I. INTRODUCTION

TABLETS

Tabletsaredefinedassolidunit dosageformscontaing medicinalsubstancewithor without suitable diluents prepared either bycompressionor moulding . Tabletsare probably the most popular dosage form. The tablet dosage form accounts for approximately 50% of all dosage forms on the market. Tablets have many advantages over other dosage forms. The majority of tablets are used in the oral administrationofdrugs, whichisthemost convenient modeofdrugadministration.

Types of Tablets CompressedTablets

Compressed tablets are prepared by single compression using tablet machines. After a quantity of powdered or granulated tableting material flow into a die, the upper and lower punchesofthe tablet machine compressthe materialunder a high pressure (~tons/in2).

MultipleCompressedTablets

Tablets may be subjected to compression more than once to prepare multiple- layered tablets or tablet-within-a-tablets (with cores and shells). In preparing layered-tablets, a portion of fill material in a die is com-pressed initially, and then anotherportionoffillmaterialisaddedtothesame die.Eachadditionalfillmaterial is compressed to formmulti-layered tablets. This is ina sense a con-trolled release device.Each portion of thefill is usually coloreddifferentlyFor the unique appearance[2]. Thepreparationoftablets having another compressedtablet as the in- ner core requires special machines which can place the preformed tablet precisely within the die for the second compression.

COATEDTABLET

SugarCoatedTablets

Compressed tablets can be coated with a sugar layer. Since the coating is water soluble, it is quickly dissolved in aqueous environment (e.g., in the gastric juice after oraladministration). The main purposes of having a sugar coating are:

(1) Toprotectthedrugfromtheairandhumidity;
(2) Toprovideatasteorasmellbarriertoobjectionable tastingorsmellingdrug.
(3) Toenhancetheappearanceofcompressed tablets.

Sugarcoatingofcompressedtabletsrequires moretimeandexpertise, andthis may increasethecostofmanufacturing.Sugarcoatingalso increasesthesizeandweight ofthecompressedtab-lets.Ifthesize oftablets is too smallthenthe sizeisincreased intention-ally by sugar coating.

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FilmCoatedTablets

Compressed tablets can be coated with a thin layer of a polymer, which may be either water-soluble or water-insoluble. The polymer film has an advantage over sugar-coating in that the polymer film is more durable, less bulky, and less time-consumingto apply.Uponoraladministration,thepolymer filmmayremain intactordissolveintheGItractdepending onthewater-solubility.

Film-coating solutions may be nonaqueousor aqueous. The nonaqueous solutions generally contain various materials to provide the desired coating to the tablets.

Requirement forwater-evaporationandareducedlikelihoodofwaterinterference with the tablet formulation. Furthermore, the low viscosity per-mits greater coat penetration into the crevices of monogrammed or scored tablets. Another commercial aqueous coating system based on ethylcellulose is Surelease® from Colorcon. ethylcellulose product is Surelease.

EntericCoated Tablets

StructuresofEnteric-CoatingMaterials

Of the many water-soluble polymers, some polymers show the property of pH-dependent water solubility. Some polymers do not dissolve at low pH (e.g., pH in the stomach) but readilydissolve at neutralpH (e.g., pH inthe intestine). Ifsuch a polymer film is coated on compressed tablets, the tab-lets willresist dissolution or disruptioninthestomachbut not inthe intestine. Suchtablets areknownasenteric coatedtablets.

TabletsCoatedwithWater-InsolublePolymers

Whena drug is loaded inside a layer ofwater insoluble polymers, the drugrelease profile fromsuchatablet different fromother compressed tablets. Theyarewidely used in the design of is often controlled release dosage forms. This topic will be discussed in more detail in the later chapters dealing with controlled release technology.

Binders(oradhesives)

Binderspromotetheadhesionofparticlesofth eformulation.Suchadhesionenables preparationofgranulesand maintainsthe integrityofthe finaltablet. Manyofthese are used as an aqueous solution in wetgranulation [2].

LubricantsandGlidants

Lubricant isasubstancecapableofreducingorpreventing friction, heat,andwear when introduced as a film between solid surfaces. It works bycoating on thesurfaceofparticles, andthuspreventingadhesionofthetablet materialto thedies and punches.

Disintegrants(orDisintegratingAgents)

The breakup of the tablets to smaller particles is important for dissolution of the drug and subsequent bioavailability. Disintegrators promote such breakup. To rupture or breakup of tablets, disintegrating agents must swell or expand on exposure to aqueous solution.

WettingAgents

Watermoleculesattracteachotherequallyina lldirections. Watermoleculesonthe surface, however, can only be pulled into the bulk water by water molecules underneath, since there are no water molecules to pull in the opposite direction.

CHITOSAN:APOLYMER

Thehistoryofchitosandiscoveredthedeacety latedformofchitin,whichwascalled chitosan. whenchitinwasboiled inaconcentratedpotassiumhydroxide solution, a product was obtained that dissolved in dilute iodine and acids, unlike chitin that only stained brown.

Natural abundance and versatility, many investigations have focused on its properties and various applications. Although studies on chitin and chitosan were initiated in the early nineteenth century, most of the reports available today on its medical and pharmaceutical applications havebeen obtained only during the last couple of decades. Despite the considerable research carried out on chitosan over recent decades, new registered products havefailed to reach the market.

Chitinisalinearpolysaccharidefoundinmarinecrustac eanshellsandthecellwalls ofbacteriaandfungi.Itisthesecondmostabundantnatur alpolymeraftercellulose.

SOURCESANDSYNTHESISOFCHITOSAN

Chitosan(pronouncedky-toe-san) isderived froma materialcalled chitin, whichis an amino polysaccharide, extracted from the powdered shells of crustaceans like shrimps and crabs. Chitosan is prepared by deacetylation of chitin. To prepare chitin, crab and shrimp shells are demineralised in dilute hydrochloric acid (HCl), deproteinated in

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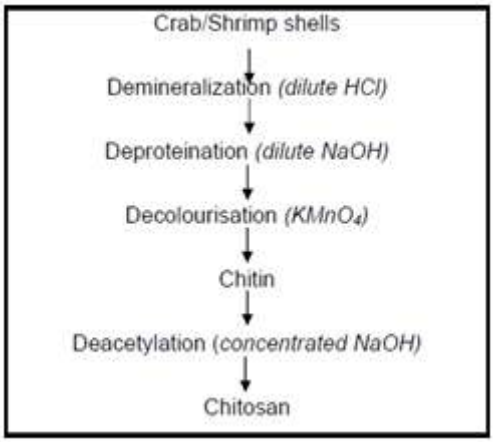
dilute sodium hydroxide (NaOH), and then decolourised in potassium permanganate (KMnO4



MATERIALANDMETHODSMATERIALSANDEQUIPMENTS
MATERIALS:

Table1:**Listofdrugandexcipient.**

Sr. No.	**Name**	**Grade**	**Specification**	**Application**
1	Aceclofenac	--	IP	NSAID
2	Chitosan	--	--	NaturalPolymer
3	HydroxyPropylMethyl Cellulose(HPMC)	K15M	--	Sustained release polymer
4	Lactoseanhydrous	--	IP	Solublefiller
5	Microcrystalline Cellulose	Avicel102	IP	Insoluble filler
8	Talc	--	--	Glident
9	Magnesiumstearate	--	--	Lubricant
10	Colloidalsilicondioxide	Aerosil200	-	Glidant
11	Anhy.CitricAcid	--	--	pHmodifier
13	Sod.bicarbonate	--	--	pHmodifier

Table2:Grades ofChitosan

Chitosan	**Degree of Deacetylation(%)**	**Viscosity** (cps)
A	84.14	37
B	88.42	93
C	89.37	51
D	92.70	52
E	96.49	49

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Table3:ListofInstrumentsandEquipments.

Sr. No.	Equipment	Manufacturer
1	Electronic Weighing Balance	Shimadzu
2	Bulk Density Apparatus	QUALITY, DBK Instruments
3	SieveShaker	EndecottsLtd.
4	SingleRotary Compression Machine	Hannainstuments
5	HardnessTester	Mansanto
6	Friabilator	Rache
7	Dissolution Test Apparatus	Labindia
8	pHmeter	METTLERTOLEDO
9	FTIR	Labindia
11	UV Spectrophotometer	Labindia
12	DSC	METTLER

APPLICATIONSOFCHITOSAN

a. Biopharmaceuticalapplications Oral drug delivery

b. Genedelivery

Thedevelopmentofnewcarriersystemsforgenedelive ryrepresentsan enabling technology for treating many genetic disorders..

Oculardrugdelivery

Thepoorbioavailabilityof topicallyappliedophthalmicdrugsimpliesa necessity for frequent instillation to achieve therapeutic effect

- **Nasaldrugdelivery**
- **Parenteraldrugdelivery**
- **Arteriosclerosis,Arterialhypertension**

ACECLOFENAC

Aceclofenac is an Non steroid anti-inflammatory drugs(NSAID). It is an orally administeredphenylaceticacidderivativeswitheffects onavarietyofinflammatory mediators.

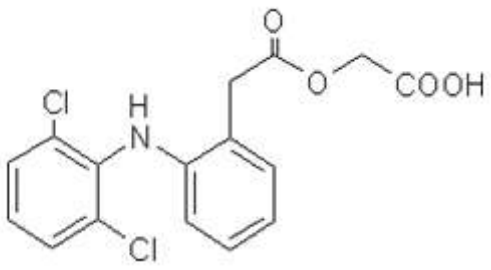

Figure1:SructureofAceclofenac.

Aceclofenaccontainsnotlessthan99.0%andnotmoret hantheequivalentof 101.0%of2-[[2-[2-[(2,6-dichlorophenyl)amino]phenyl]acetyl]oxy]acetic acid. Itisawhiteoralmost

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whitecrystallinepowder.Aceclofenacprovidessympt omatic relief in a variety of painful conditions.

a. Pharmacokinetics:

Aceclofenacisrapidlyandcompletely absorbedafteroral administration,peak plasma concentrations are reached 1to 3 hours after anoraldose.
ofeachdoseofAceclofenac,20%isexcretedinthefaece s.Theplasma elimination half-life of the drug is approximately 4hours.

b. DrugInteractions:

- Aceclofenacmayincreaseplasmaconcentrat ionsofLithium,Digoxinand Methotrexate
- increase the activityofanticoagulant
- inhibits the activity of diuretics
- enhancecyclosporin nephrotoxicityand precipitateconvulsions whenco- administered with Quinolone antibiotics.

c. DosageandAdministration:

TheusualdoseofAceclofenacis100 mggiventwicedailybymouth,onetabletin the morning and one in the evening.

Uses:

➢ **Aceclofenac-ClinicalEfficacy**

Aceclofenac reduced painandimproves functionalcapacityand mobilityrelative to baseline in patients with osteoarthritis, rheumatoid arthritis or ankylosing spondylitis and reduces inflammation in patients with rheumatoid arthritis.

➢ **Aceclofenacinosteoarthritis**

In patients with osteoarthritis of the knee, Aceclofenac decreases pain, reduces disease severityandimproves thefunctional capacityofthe knee .

Aceclofenacinrheumatoidarthritis

The anti-inflammatory and analgesic efficacy of Aceclofenac is similar to that of Ketoprofen,Indomethacin, Tenoxicamand Diclofenac inpatientswithrheumatoid arthritis.

Aceclofenacindentalpain

TheanalgesicefficacyassingledosesofAcecl ofenachasbeenassessedinpatientswithmoderate to severe tooth pain and in extraction of impacted third molars.

II. RESULTAND DISCUSSION

Preformulationstudy

Solubilitydeterminationofdrug

The available literature on the solubility profile of Aceclofenac indicates that the drugis freely soluble in acetone and practically insoluble in water. In the present study, Aceclofenac showed pH-dependent solubility; as pH was raised from 1.2 to 6.8, solubility improved considerably

Quantityof Aceclofenac	Quantityofsolvent	Inference(mg/mL)
100mg	100mLofwater	0.057±0.010
100mg	100mLofacetatebufferpH4.5	0.184±0.010
100mg	100mLof0.1NHCl	0.012±0.010
100mg	100mLofphosphatebufferpH6.8	0.784±0.010

Table4: SolubilitystudyofAceclofenac

Determination ofλmax

Anaccuratelyweighedamount(10mg)of Aceclofenacwasdissolvedinphosphate bufferpH6.8,withconstant shakingtillit dissolvedcompletelyand makingthe volume up to 100 mL toget stock solutionof100 µg/mL.Dilution was done to obtai50 µg/mL solution. This solutionwastakenas standard and wasscanned photometrically between 200-400 nm using phosphate buffer pH 6.8 as blank. The λmax was determined and found to be 274 nm.

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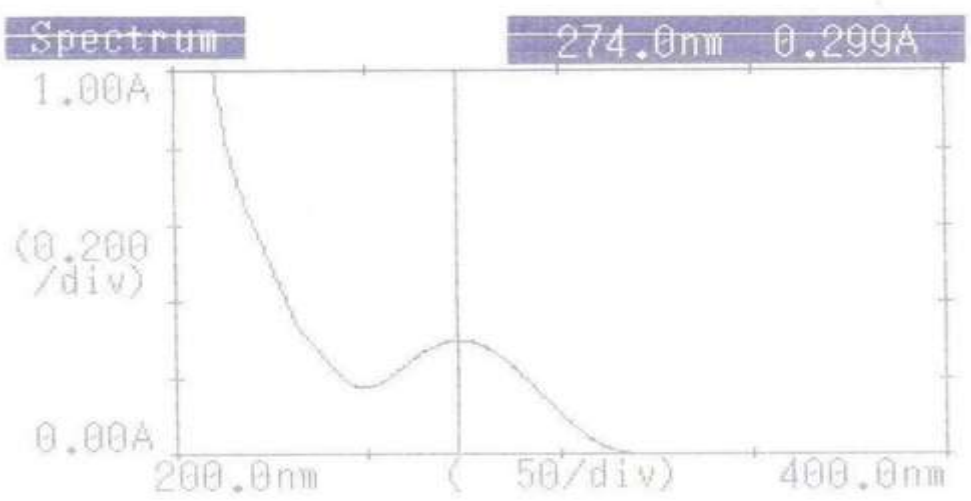

Fig-UVspectra forAceclofenac

IRSpectroscopy(IR)study

The characteristic peaks of Aceclofenac in matrix tablets were observed at the bands 3457cm^{-1} (N-H stretch), 1725cm^{-1} (C=O (esteric) stretch), 1680 cm^{-1} (C=O (carboxylic) stretch), 1349 cm^{-1} (C=C stretch), 826 cm^{-1} (C-Cl stretch), 680 cm^{-1} (aliphatic C-H band)for Aceclofenac.

Thecharacteristicpeaksat3352cm^{-1}(N-Hstretch),3202cm^{-1}(O-Hstretch),1143cm^{-1}(C-Ostretch), 761cm^{-1} (C-Hdef) wereobservedand assigned for ChitosanAandB. Peak for ChitosanCwereobservedat 3486.67cm^{-1} (N-Hstretch), 2983.34cm^{-1} (O-H stretch), 1655 cm^{-1} (C=O stretch), 1370.18 cm^{-1} (C-N stetch), 662.42 cm^{-1} (C- H def) The physical mixture of Aceclofenac with Chitosan, HPMC K15M clearly shows the retention of these characteristic peaks of Aceclofenac thus revealing no interaction between the selected drug and polymers.

CharacteristicpeaksofChitosaninFTIR

Sr.No.	Functionalgroup	Correspondingpeak(cm^{-1})
1	N-Hstretch	3486.67
2	O-Hstretch	2983.34
3	C=Ostretch	1655
4	C-Nstretch	1370.18
5	C-Ostretch	1151.29
6	C-Hdef	662.42

CharacteristicpeaksofHPMCin FTIR

Sr.No.	Functionalgroup	Correspondingpeak(cm^{-1})
1	O-Hstretch	2973
2	C-Ostretch	1155.15
3	C-Cstretch	1256.3
4	C-Hdef	627.71

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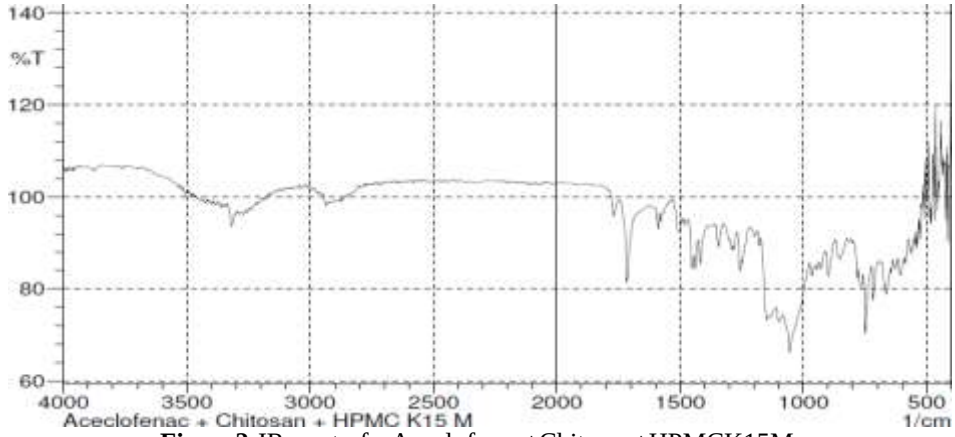

Figure2:IRspectraforAceclofenac+Chitosan+HPMCK15M.

Table5:CharacteristicpeaksofAceclofenacinFTIR

Sr.No.	Functional group	Correspondingpeak ofplaindrug(cm^{-1})	Correspondingpeak ofmixture(cm^{-1})
1	N-Hstretch	3352	3352
2	O-Hstretch	3202	3202
3	C-Nstretch	1390	1390
4	C-Ostretch	1143	1143
5	C-H def	761	761

Aspeaksofdrugandmixtureofdrugandpolymerswere obtainedatsamewavelengths thereforewecanconcludethatthereisnointeractionbet weendrugandpolymersused.

7.1A.4:DSCstudy

Asharpendothermicpeak wasobserved for Aceclofenac (Tpeak=154.2°) at theroom temperature corresponding to its melting point 150-158°. The characteristic, well- recognizable thermalprofile ofthe drug appeared at the temperature corresponding to its melting point in the Aceclofenac - Chitosan matrix tablet showing thermal peak at 152.0° .

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DSCthermogramforAceclofenac+ChitosanC.

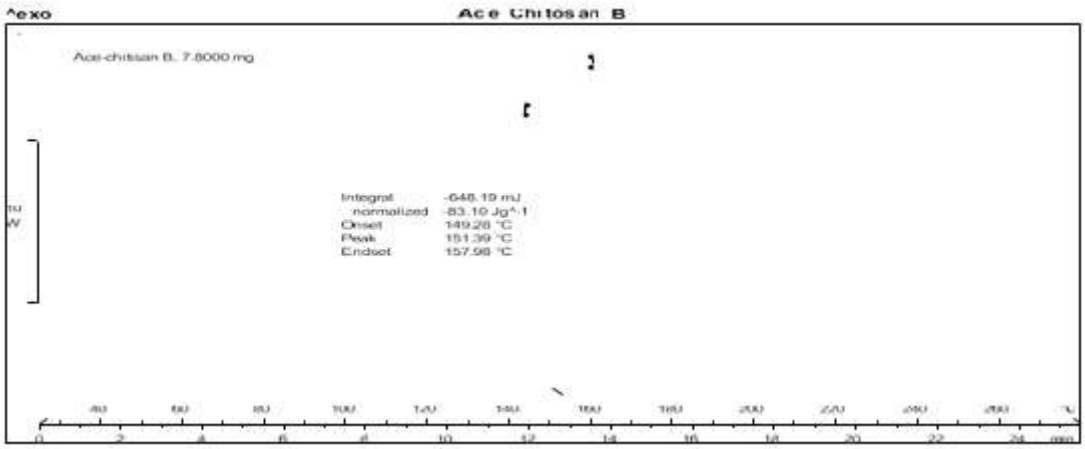

Figure3:DSCthermogramforAceclofenac+Chitosan+HPMCK15M

Construction ofstandardcalibrationcurve

Standardcalibrationcurve in6.8pHphosphatebuffer wasconstructed usingthe stock solution of 100 µg/mL. The samples were scanned for λmax at the UV rangeof 200- 400 nm. After 1 day again the samples were scanned for λmax

Table6: Absorbancevaluesforthecalibrationcurveof Aceclofenac(5-40µg/mL).

Sr. No.	**Conc.(**µg/mL**)**	**Absorbance**
1	5	0.120
2	10	0.241
3	15	0.363
4	20	0.485
5	25	0.584
6	30	0.729
7	35	0.850
8	40	0.972

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CorrelationCoefficient (R)	0.9996
Slope	41.1225
Intercept	0.1705

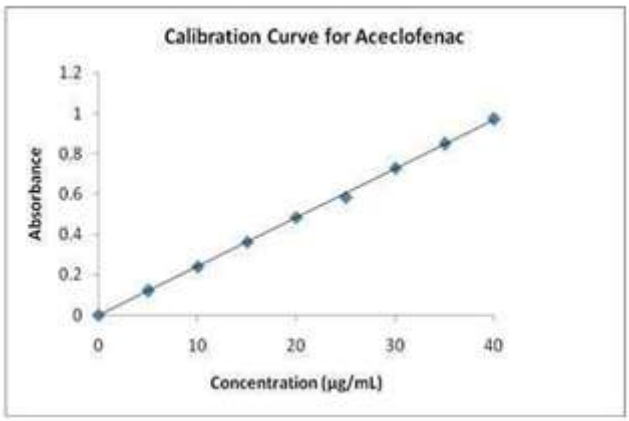

Figure4: Calibrationcurve forAceclofenac

FormulationofmatrixtabletsofAceclofenaccontainingChitosanandHPMC.

Evaluation
Evaluationofgranules:

Table7: Pre-compressionevaluationofthelubricatedblend.

Sr. No.	BulkDensity (g/mL)	TappedDensity (g/mL)	Carr'sIndex (%)	Hausner's Ratio
1	0.501±0.002	0.554±0.004	09.560±3.216	1.106±0.006
2	0.641±0.003	0.881±0.004	27.24±3.163	1.375±0.005
3	0.532±0.003	0.726±0.005	26.720±1.068	1.365±0.001
4	0.541±0.003	0.833±0.003	35.05±1.654	1.541±0.002
5	0.515±0.002	0.636±0.001	19.020±1.204	1.235±0.054
6	0.527±0.002	0.602±0.001	12.450±1.248	1.142±0.001
7	0.575±0.007	0.855±0.002	32.74±1.457	1.488±0.023
8	0.547±0.004	0.794±0.025	32.97±1.042	1.455±0.057
9	0.553±0.050	0.632±0.083	12.500±1.538	1.143±0.051
10	0.545±0.045	0.860±0.004	36.620±1.048	1.578±0.045
11	0.502±0.013	0.775±0.005	35.220±1.078	1.545±0.003
12	0.566±0.006	0.875±0.004	35.31±1.238	1.546±0.160
13	0.506±0.014	0.569±0.016	11.070±1.045	1.125±0.021
14	0.511±0.063	0.665±0.012	23.15±1.016	1.302±0.004
15	0.508±0.003	0.683±0.048	25.62±1.489	1.346±0.048
16	0.505±0.013	0.701±0.081	27.96±1.010	1.389±0.156
17	0.584±0.0058	0.908±0.054	35.68±1.104	1.555±0.041

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18	0.514±0.035	0.576±0.078	10.76±1.848	1.121±0.010
19	0.515±0.043	0.698±0.051	26.21±1.768	1.356±0.201
20	0.511±0.023	0.702±0.048	27.20±1.193	1.374±0.057

*****Mean±S.Dforn=3

The prepared granules were evaluated for different properties like Bulk density, Tap density,Carr'sIndexandHausner'sratio(Table23)and alltheparameterswerefound to be in good agreementwith the standards.

The formulated tablets were evaluated for weight variation, thickness, friability, hardness, disintegrationtest, drug content .And allthe parameters were found to be ingood agreementwiththe standards.Swellingstudiesand In-vitrodrugreleasestudieswerecarriedoutandillustrated throughTable8-9 andFigure 5 respectively.

Evaluationoftablets

Table8:Post-compressionevaluationparametersofmatrixtabletsofAceclofenac with Chitosan and HPMC.

Sr.No	**Weight Variati on(%) (±SD)**	**Thickness (mm.)(±SD)**	**Friability (%)(±SD)**	**Hardness (Kg./cm^2)(±SD)**	**Dru g content (%)(±S D)**
1	0.151±0.165	4.32±0.125	0.3±0.187	4.03±0.05	97.56±1.73
2	0.202±0.223	4.20±0.123	0.23±0.163	5.16±0.665	97.63±2.35
3	0.423±0.107	4.23±0.214	0.2±0.369	5.15±0.162	98.76±1.65
4	0.725±0.040	4.13±0.363	0.5±0.353	5.15±0.262	99.43±1.66
5	0.247±0.516	4.46±0.221	0.5±0.620	4.16±0.546	98.45±2.65
6	0.215±0.035	4.40±0.141	0.4±0.165	4.54±0.521	97.81±2.98
7	0.584±0.253	4.54±0.110	0.7±0.202	4.16±0.453	98.32±3.01
8	0.532±0.321	4.28±0.643	0.4±0.601	5.21±0.135	98.79±2.58
9	0.513±0.840	4.36±0.303	0.4±0.415	5.56±0.136	98.56±1.99
10	0.218±0.535	4.26±0.100	0.5±0.463	4.62±0.164	99.10±1.70
11	0.251±0.135	4.38±0.233	0.6±0.189	4.41±0.427	99.42±2.00
12	0.846±0.354	4.21±0.043	0.5±0.161	5.12±0.156	98.09±2.67
13	0.469±0.452	4.12±0.464	0.1±0.068	5.16±0.148	97.45±0.73
14	0.469±0.452	4.12±0.464	0.1±0.068	5.16±0.148	97.45±073
15	0.523±0.157	4.14±0.347	0.2±0.187	4.73±0.199	98.41±0.65
16	0.106±0.102	4.06±0.222	0.1±0.247	4.56±0.365	97.12±0.27
17	0.500±0.389	4.16±0.101	0.5±0.162	4.67±0.543	99.42±0.52
18	0.342±0.335	4.32±1.109	0.3±**0**.115	5.14±0.194	98.25±2.32
19	0.542±0.153	4.22±0.169	0.8±0.653	4.61±0.163	99.41±.96
20	0.532±0.045	4.36±**0.**141	0.9±0.143	4.46±0.489	99.23±1.65

Tableshowspost-compressionalparameters i. e. hardness, friability, weight variation and thicknessanddrugcontents..Hardness, friability,weightvariation,thicknessanddrug content was found to be within the acceptable official limits.

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Table9: Drugrelease(%)ofmatrixtablets1.

Time (Min)	Drugrelease(%)								
	1	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**
0	0	0	0	0	0	0	0	0	0
30	18.21± 0.585	12.06± 0.387	31.33± 1.006	13.35± 0.429	14.25± 0.457	10.68± 0.343	21.04± 0.675	45.21± 1.45	88.33± 2.835
60	27.81± 0.893	17.44± 0.560	42.25± 1.356	18.72± 0.601	19.05± 0.612	25.34± 0.813	41.22± 1.323	57.27± 1.20	98.31± 1.190
120	39.12± 1.256	26.04± 0.836	65.55± 2.104	29.25± 0.939	38.07± 1.222	30.22± 0.970	51.36± 1.649	77.52± 1.62	98.45± 0.197
180	70.41± 1.479	48.22± 1.548	72.75± 1.528	49.12± 1.577	54.56± 1.751	41.21± 1.323	59.25± 1.902	89.22± 0.89	99.21± 0.208
240	90.18± 1.849	61.36± 0.681	88.32± 0.980	64.26± 2.063	67.04± 0.744	51.51± 1.653	66.32± 0.736	92.01± 0.92	99.78± 1.108
300	98.65± 0.987	79.25± 1.11	94.53± 1.323	84.32± 0.843	88.34± 1.237	62.22± 1.997	80.31± 1.124	95.61± 1.14	99.78± 1.397
360	99.54± 0.995	86.32± 1.062	99.47± 1.223	90.14± 1.082	92.01± 1.132	72.18± 1.588	94.44± 1.162	99.65± 0.99	99.82± 1.228
420	99.87± 1.198	90.31± 0.271	99.9± 0.300	96.68± 1.189	98.75± 0.296	80.31± 0.972	98.36± 0.295	99.99± 1.00	99.92± 0.300
480	99.91± 0.999	98.44± 0.098	99.99± 0.100	99.211 ±200	99.24± 0.099	95.12± 0.200	99.9± 0.100	99.99± 1.00	99.95± 0.100

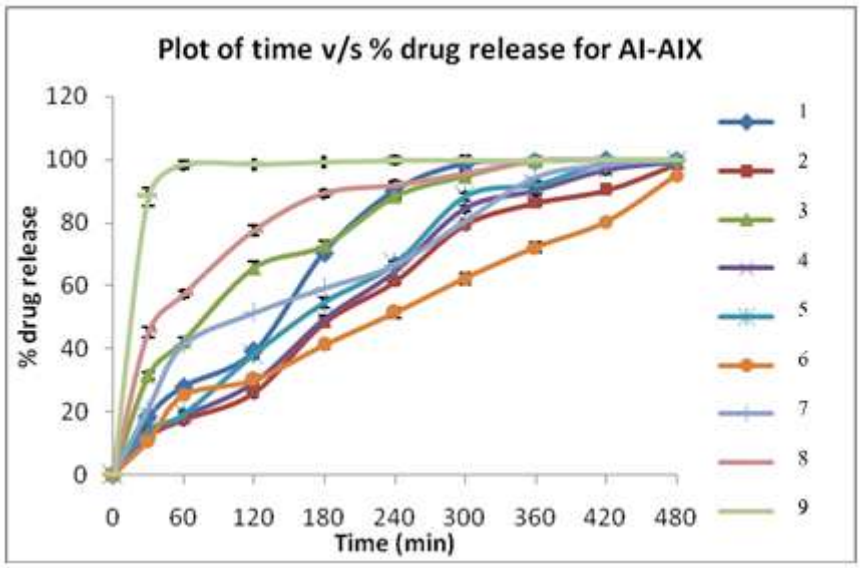

Figure5: Plotoftimevs.%drugreleasefor1to9.

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StabilityStudies

TheselectedformulationswerekeptforAccelerated stabilityat40°C2°C75%RH5% RH. The sampleswere withdrawn at aregular time interval. The ± formulationswere testedfordifferentparameterslike%drugcontentsandcumulativedrugreleasewere measured and the results of accelerated stability studies are shown in **Table 10-11** No significantchanges ± in anyofthe above parameters were observed. The formulations were found to be quite stable

Table10: AssayoftabletskeptforAcceleratedStabilityStudies

Formulation Batch	DrugContent(%)				
	Initial	1Month	2Months	3Months	6Months
1	98.52±1.92	98.59±1.80	98.52±1.92	98.32±1.72	98.22±1.12
2	97.51±1.59	97.55±1.60	97.51±1.59	97.61±1.39	97.41±1.34
3	98.65±2.15	98.45±1.90	98.65±2.15	98.45±1.15	98.87±1.05
4	99.65±1.87	99.15±1.77	99.65±1.87	99.55±1.67	99.75±1.41

* Mean±S.D forn=3

Table11: DissolutionprofileoftabletskeptforAcceleratedStabilityStudies

Formulation Batch	DrugRelease(%)after480min.				
	Initial	1Month	2Month	3Months	6Months
1	95.12±0.25	96.33±0.27	96.50±0.28	97.45±0.55	97.13±0.65
2	97.25±1.94	97.50±0.1.95	96.10±1.25	97.95±1.65	98.46±01.25
3	97.30±0.25	96.86±0.35	96.10±1.30	96.22±0.85	97.20±0.65
4	91.23±0.24	92.10±0.26	92.62±0.45	94.50±0.55	94.16±0.45

No significant changes with respect to any of the physiaclparameters likecolour and hardnessofthetabletsandalsoaboveparameterswereobserved.The formulations were found to be quite stable.

III. CONCLUSION

PhysicochemicalpropertiesofAceclofenacwerestudiedandfoundthatalltheparameterswerein the prescribedlimit.

Preformulation studies viz. solubility studies, determination of λ max (UV), Identificationstudy(FTIR),thermalstudies(DSC)werecarriedouttocheckpurity andqualityofdrugsused.

FromsolubilitystudiesitwasfoundthatAceclofenacshowedpH-dependent solubility;aspHwasraisedfrom1.2to6.8,solubilityimprovedconsiderably. (0.057and 0.784 mg/mL in water and phosphate buffer (pH 6.8) respectively.)

For determination of **λmax** 50 µg/mL solution in Phosphate buffer (6.8) was Scannedphotometricallybetween200-400nm.Theλmaxwasdeterminedandfound to be 274 nm.

In identification study using **FTIR** it was observed that characteristic peaks of Aceclofenac were observed at the bands 3457cm^{-1} (N-H stretch), 1725cm^{-1} (C=O (esteric) stretch), 1680 cm^{-1} (C=O (carboxylic) stretch), 1349 cm^{-1} (C=C stretch),826 cm^{-1} (C-Clstretch),680cm^{-1} (aliphaticC-H band).Theresult confirmsthe identityand purityof drug,Aceclofenac.

1) a) Studyofdrug-polymer **incompatibility** revealedthat no significant changes in intensity of the FTIR bands of Aceclofenac were observed with polymers indicating the absence of interaction.

b)Thebaselineinthe**DSCthermogram**wasobserved withabsenceofanyexothermic peak.Theabsenceofexothermic peaks clearly

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indicatesthestabilityofthe mixture. It was also interesting to notethat the end peak was found to be at 156-158forallthephysicalmixturesensuringnophysicalinteractionbetweenAceclofenac and polymers.

2) Present study involved the use of Chitosan as a release rate modifier as against HPMC. Aceclofenac is an orally effective non-steroidal anti-inflammatory drug (NSAID) of phenyl acetic acid group. Unfortunately, Aceclofenac suffers from low aqueous solubility (0.058 µg/ml), leading to poor dissolution and insufficient oral bioavailability. Aceclofenac is an example of BCS class II compound, its oral bioavailability is determinedbydissolution rate in the gastrointestinal tract.

3) From the drug release rate study it can be noted that formulations having only ChitosanactswellaloneasreleasemodifierasagainstHPMC,Chitosanhavinghighest degreeofdeacetylation(DAD) (E-95%) isa betterrelease modifier thanthosehaving lower DAD and Viscosity also plays an important role in retarding the drug release fromthe matrix.

Toestablishthe**significanceoftheuseof Chitosan**asareleaseretardant polymerasagainstHPMC,thedataobtainedwasanalyzedusing**Minitab*** software **Swelling behavior of matrix tablets**

When swelling studyof formulations were carried out it was observed that Chitosan matricespreferentiallyundergo radialswelling as compared to axialswelling. Several important features regarding the development of the gel layer are noted. First, a continuous increase in the gel layer thickness is observed irrespective of the polymer viscositygrade or substitution ratio.

*Thehigherconcentrationleadstoincreasedcontactpointsbetweenadjacent Chitosan particles with minimum of interruptions. This leads to formation of uniform gel structure with enhanced gel strength. Hence, the release becomes progressively swelling-erosion dependent. When swelling study of formulations were carried out it wasobservedthat Chitosan matricespreferentiallyundergo radialswelling ascompared to axial swelling. Neither the water soluble filler Lactose nor the water insoluble excipientMicrocrystalinecellulose (MCC) affect this behaviorofChitosanasdiscussed in the previous section.

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