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RESEARCH ARTICLE

ROLE OF FUNCTIONALIZED GUAR GUM IN SOLID DISPERSION OF NON-STEOIDAL ANTI-INFlAMMATORY DRUG

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Abstract

The current investigation was developed to study the role of functionalized guar gum as carrier in solid dispersion of iboprofen. The solid dispersion technique using aminated guar gum would be an effective approach for increasing the solubility and increasing dissolution behaviour of ill fathomable medicament than the native guar gum. The results of FTIR and DSC studies confirmed that there is no chemical interaction or no incompatability between the drug and excipients. The invitro dissolution study was performed for the the prepared formulations. Based on the results SD3 was shown highest drug release 99.41% within 24hrs. Stabiliy study was conducted as per ICH guidelines and the falloutsrevealed that there is no physical or chemical change.it may be concluded that solubility of ibuprofen can br improved by using functionalized guar gum in the solid dispersion, which provides a wide scope for the therapeutic efficiency.

Introduction:-

SolidDispersion: The term strong scattering alludes to a gathering of strong items comprising of somewhere around two parts, by and large a hydrophilic grid and a hydrophobic medication. The lattice can be either glasslike or nebulous. The medication can be scattered microscopically, in nebulous particlesorincrystallineparticles.[1]

Oral availability of medication relies upon its solvency or potentially disintegration rate, in this way serious issues related with these medications was its very dissolvability in natural liquids, which results into helpless bioavailability after oral organization. Numerous techniques are accessible to further develop disintegration rate, dissolvability attributes, including salt arrangement, micronization and expansion of dissolvable or surface dynamic specialists. The term strong scattering alludes to a gathering of strong items comprising of somewhere around two parts, by and large a hydrophilic network and a hydrophobic medication. The lattice can be either glasslike or nebulous. The medication can be scattered microscopically, in formless particlesorincrystallineparticles.2Strong scattering is one othese strategies, which was most broadly and effectively applied to work on the solvency, disintegration rates and thus the bioavailability of inadequately solvent medications. The idea of strong scatterings (SDS) was presented in 1961 by Sekiguchi and Obi, in which the medication is scattered in inactive water-dissolvable transporter at strong state. Several water soluble carriers such ashydroxyl propyl methyl cellulose, ethyl cellulose, beta cyclodextrin, urea, lactose,citric acid, poly vinyl pyrrolidone(PVP) and poly ethylene glycols such as carriersforSolid dispersion

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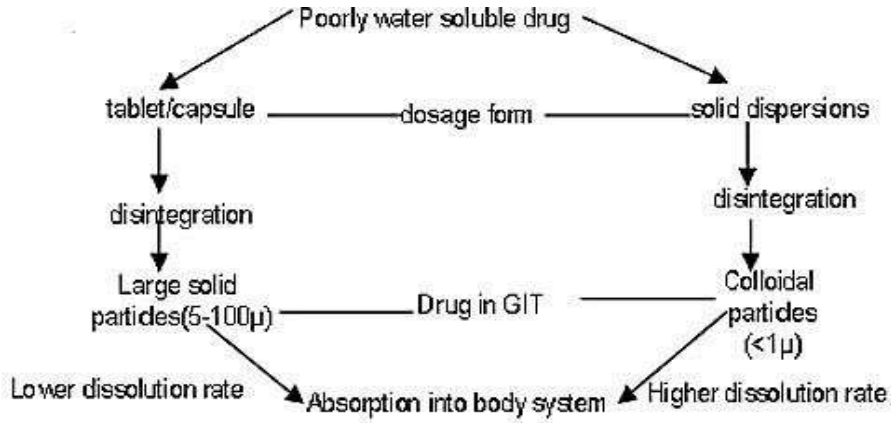

Figure 1:- Schematic representation of the bioavailability improvement of ineffectively water solubledrugbysolid dispersion technique.[4]

Naturalcarrier

More hydrophilic nature of carriers enhances the faster release of drugsfrom solid dispersion. A poor water soluble or insoluble carriers may leads toslowerreleaseof drug

Guar gum is a galactomannan, obtained from plant Cyamopsis tetragonolobus. Powder is whitish and yellowish consisting of slight odor. Guar gum is mainly consisting of thehigh molecular weight polysaccharides composed of galactomannans which are consisting of a linear chain of (1→4)-linked β-D-mannopyranosyl units with (1→6)-linked α-D-galactopyranosyl residues as side chains. The mannose: galactose proportion is roughly 2:1. The atomic weight territory is 50,000-8,000,000.

Amination of Natural gums

Recently,chemical modification or derivatization of natural polysaccharides hasbeen reportedto improve the functional propertiesof native gums.Reports in the literature suggestthatthe derivatives of polysaccharides (amine, thiol, carboxymethyl) can be employed tomanipulateswelling, bioadhesion and drugrelease A couple of instances of polysaccharide subsidiaries previously revealed in writing incorporate N-(2-hydroxy) propyl-3-trimethyl ammonium chitosan, glycol chitosan, n-succinyl chitosan, thiolated hydroxyl ethyl cellulose carboxymethyl tama-rindkernelpowder,aminated tamarindkernel polysaccharide, thiolatedchitosan.

Materials and Methods:-

Chemicals Used

Ibuprofen, Guar gum, Ethylene diamine, Sodium Bromide, Ethyl alcohol procured from Loba Chem. Mumbai, India.

Instruments Used

AnalyticalBalance (Shimadzu, Japan.), FTIRSpectrophotometer (JascoFT-IR8201PC), DissolutionApparatus (Electro labTDT-08L), DifferentialScanningCalorimetry (PerkinElmer,Pyris6DSC,Germany), UVSpectrophotometer (U.V 1700 Shimadzu, Japan.) and Hotairoven (Thermolab)

Preformulation Studies

Construction ofStandard GraphofIbuprofeninpH7.4Phosphatebufferbyusing theUVmethod

100mg of ibuprofen was weighed and transfer into a 100ml of volumetricflask and was dissolved in phosphate buffer of pH7.4 and make up to 100ml.Thiswas the standard stock solution containing 1mg/ml of ibuprofen.From this stock arrangement, 10ml was taken and made up to 100ml with phosphate cushion pH 7.4.This was the second standard stock solution (100µg/ml).From this solutiondilutionsof10µg/ml,20µg/ml,30µg/ml,40µg/ml,50µg/mlweremadeandabsorbance wasmeasured at 222nm.

Synthesis of Functionalized Guar gum

AminationofGuargum

In 3000ml water add 60gm of Natural Guargum. To this solution add aminating agent ethylene diamine (25ml) with continuous stirring at constant temperature (20-60^{0}C) for 6 hr. then slowly add reducing agent Sodium Bromide ($NaBH_4$) for 2hrs until formation of thick gel. Wash this gel several times with ethyl alcohol and collect the precipitate of aminated derivative of Guar gum.

PreFormulationStudies

Appearance

Colour and physical state of the drug is done by Visual examination.

Melting point

Melting point of the Ibuprofen was resolute by capillary method in triplicate.

Solubility determination study

The dissolvability of Ibuprofen was dictated by the harmony dissolvability technique in which a soaked arrangement of the material was gotten by blending an overabundance of medication in a steady amount of dissolvable until immersion or balance was accomplished in a vortex blender. Then, at that point it was separated through Whatman channel paper (no.1) and focus was investigated by UV spectrophotometer at 222 nm. The dissolvability of not really set in stone in refined water and pH across the gastrointestinal plot, for example in pH 1.2, 6.8, and 7.4.

DifferentialScanningCalorimetry(DSC)

Thedifferentialscanningcalorimetry(DSC)ofpuredrugs,soliddispersion,andthephysicalmixtureoftheremedy wasperformedusingDSCinstrument (Perkin Elmer Pyris 6 DSC, Germany), for the measurement of heatloss or gain resulting from physical or compound changes inside the example as a component of temperature. Around 6-7 mg of the example was made an appearance aluminum DSC container and hermetically sealed with aluminium lids. An underlying incline was utilized to hop the temperature to 30ºC and afterward a steady warming pace of 10ºC/min was utilized something like 400ºC under nitrogen temperature.

FourierTransformInfrared(FTIR)studies

The similarity of medications and excipients utilized under trial condition were contemplated. The examining range was 400 to 4000 cm-1 and the goal was 1cm-1. This unearthly examination was utilized to check the similarity of medications with the excipients utilized and put away.

Powder X-ray diffraction

Powder X-beam diffraction studies were performed to check for any crystallinity in the definition after it was made and after the strength studies were performed. Staying away from recrystallization of the medication in the definition was one of the objectives of the current investigation. Skillet logical X-Pert Pro V1.6 with X Pert Data Collector V2.1 programming was utilized furnished with a CuKa2 anode cylinder and diffractometer of span 240 mm. The X-beam powder diffraction check was performed utilizing a BB004 level stage. The powdered example was put in an aluminum test holder that had a 2.5 cm square with a profundity of 0.5 mm. The information were gathered by filtering the example at 45 kV and 40 mA. Tests were filtered from 5 to 50°C 2θ at a stage size of 0.0170 and output pace of 1.0°C/min.

FormulationDevelopment

PreparationSoliddispersionofIbuprofen

Preparation of solid dispersions of Ibuprofen is to improve the solubility ofIbuprofen and dissolution rate. Solid dispersion of Ibuprofen was prepared byhot melt method. The drug and carrier were mixed in 1:1, 1:2 and 1:3ratios in ethanol. Solventwas removedby evaporation under reduced pressureThe mass was crushed and gone through strainer no 60

PreparationofphysicalmixturecontainingIbuprofen

Thecorporeal assortments of Ibuprofen-guar gum and Ibuprofen Aminated guar gum in the identicalheft ratio (1:3) were primed by scrupulously mixingthe appropriate amount of two components for 10 min in a mortar. The concoctionsweresievedthrougha60meshscreenandstoredinadesiccatorforfurtherevaluation.Solid dispersions were prepared by hot melt method. Correspondingphysical mixtures were heated in an oil bath at 175^{0}Cuntil they melted.

Solidification was reached by cooling to room temperature under ambient conditions. Afterwards, the mixture was pulverised, sieved, and thefraction≤160µm wasselected.The methodofpreparationandcompositionwere givenTable1.

Table 1:- Composition of various batches of Physical mixturesandIbuprofen SolidDispersion.

BatchCode	Composition	Ratio
S.D1	Ibuprofen:Aminated guar gum	1:1
S.D2	Ibuprofen:Aminated guar gum	1:2
S.D3	Ibuprofen:Aminated guar gum	1:3
S.D4	Ibuprofen:guar gum	1:1
S.D5	Ibuprofen:guar gum	1:2
S.D6	Ibuprofen:guar gum	1:3

EvaluationofIbuprofensoliddispersionsandcorporeal mixtures
Evaluationstudieswerecarriedoutbyestimatingdrug contentand*invitro*dissolutionstudies.

Determination of solubility of various solid dispersions
Ibuprofen laden strong scatterings, actual combinations, and unadulterated Ibuprofen identical to 30 mg were gauged and moved to four cups containing 50 mL of refined water, pH 1.2 acetic acid derivation cushion, phosphate support pH 6.8, and phosphate cradle pH 7.4. The example was fomented at 80 rpm in a thermostated shaking water shower at 37±0.5°C for 8 h. The supernatant arrangement was then sifted through Whatman channel paper. The filtrate was weakened and the absorbance was estimated utilizing an UV-Vis spectrophotometer.

Drugcontent
The drug content of each solid dispersion physical mixture weredetermined by UV-spectrophotometry. Accurately weighed quantity of samplesfrom all batches equivalent to 100 mg of Ibuprofen was transferred to a 100mlvolumetric flask containing 100ml of phosphate buffer pH 7.4 and the absorbancewasmeasured at 222nm.

Invitrodissolutionstudies
Thepreparedsoliddispersionswereaccuratelyweightequivalentto100mgofthedrug.Thesesoliddispersionsarefilledinemptycapsulesand analysed for drug release in 900ml of phosphate buffer pH (7.4) as dissolutionmedium at 37± 0.5ºC and 50rpm. 5ml of the sample solution was taken from thedissolutionapparatusandthesamevolumereplacedwithfreshdissolutionmediumatpredeterminedtimeintervalsfor5min.Theabsorbanceofthesesolutionswasmeasuredat 222nmusingUV-Visiblespectrophotometer.

Stabilitystudies
Stability study was carried out to observe the effect of temperature andrelative humidity on selected formulation (SD3), by keeping at 40±2ºC, in air tighthighdensitypolyethylenebottlesforsixmonths,atRH75±5%.Physicalevaluationwascarried out ineach month.[9]

Table2:- ICHguidelinesforStabilitystudy.

Study	Storagecondition	Timeperiod
Longterm	25ºC±2ºC/60%RH±5%RH	12month
Intermediate	30ºC±2ºC/65%RH±5%RH	6 month
Accelerated	40ºC±2ºC/75%RH±5%RH	month 6

Results and Discussion:-

PreparationofCalibrationcurveforIbuprofen
Table 3:- CalibrationcurveofIbuprofen.

Concentration(µg/ml)	Absorbance(222nm)
0	0
10	0.151
20	0.351
30	0.521
40	0.713
50	0.912

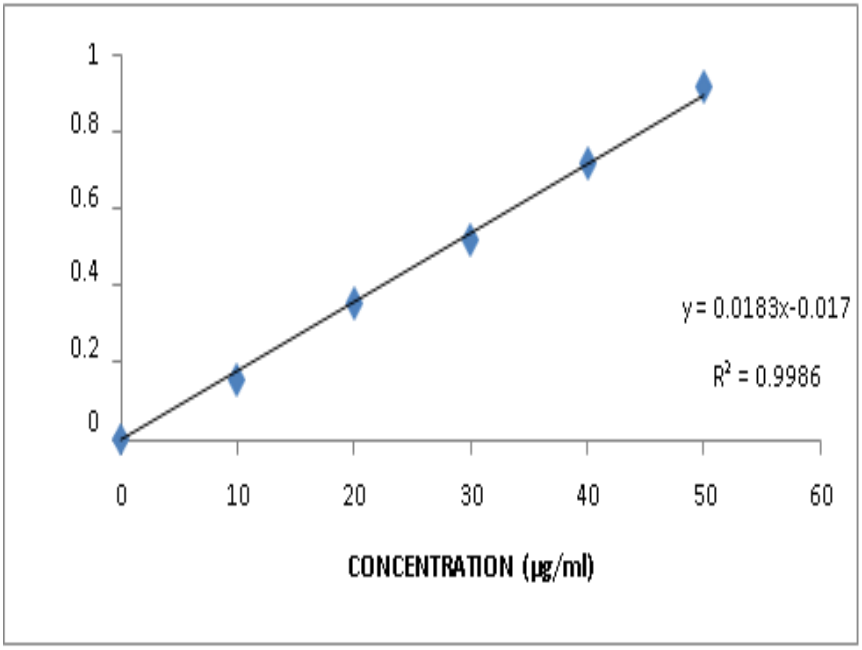

Figure 2:- Calibrationcurveofibuprofen.

The calibration curves were linear and obeyed Beer-Lambert's law in theconcentration range 10-50µg/ml. The correlation coefficient values were 0.9986indicatingexcellent linearityof thedata.

Appearance
Ibuprofenappeared as crystalline solid.

Melting point
Melting point of drug was determined by capillary method. The result is found to be 75-77^{0}C.

Saturation solubility

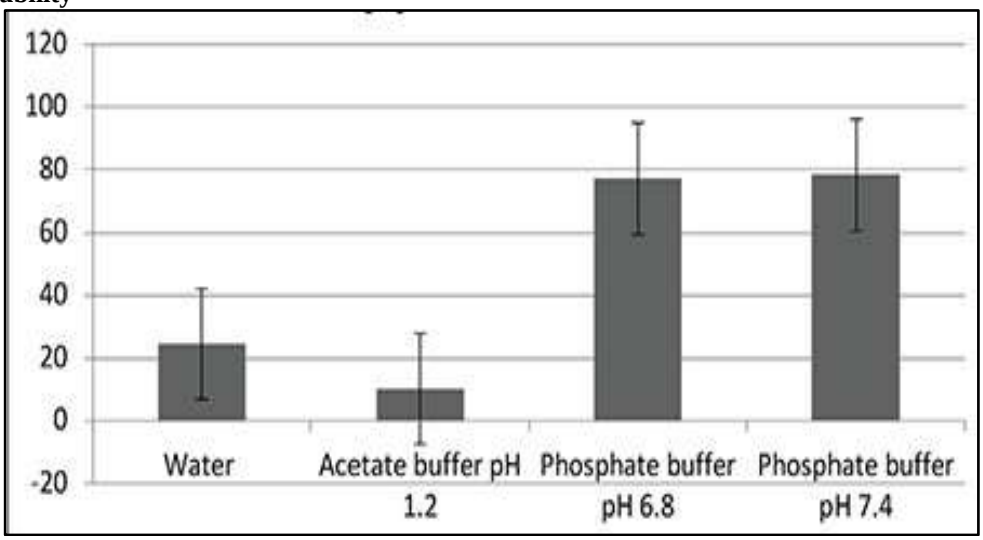

Figure 3:- Graphical representation of Solubility data of Ibuprofen in different solvents.

The solubility data of Ibuprofen in distilled water, Acetate buffer pH 1.2, phosphate buffer pH 6.8, and phosphate buffer pH 7.4 at 25°C are given in Table 11. The comparison of Ibuprofen in different solvents is presented graphically in Figure 15. From the Results we can conclude that the drug is poorly soluble in nature. So is suitable for the formulation of Solid disperssion toenhance itssolubility.

CompatibilityStudies
DifferentialScanningCalorimetry(DSC)

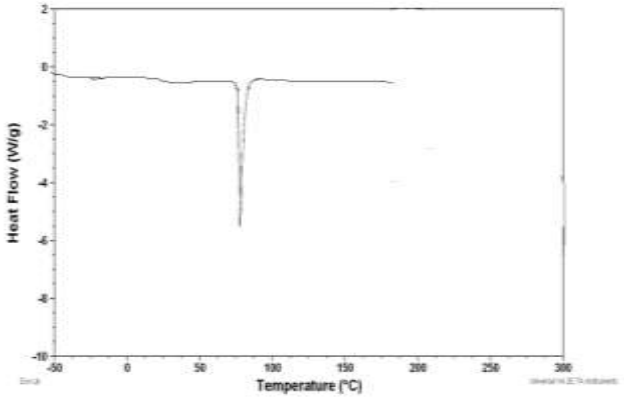

Figure4:-DifferentialScanningCalorimetryofIbuprofen

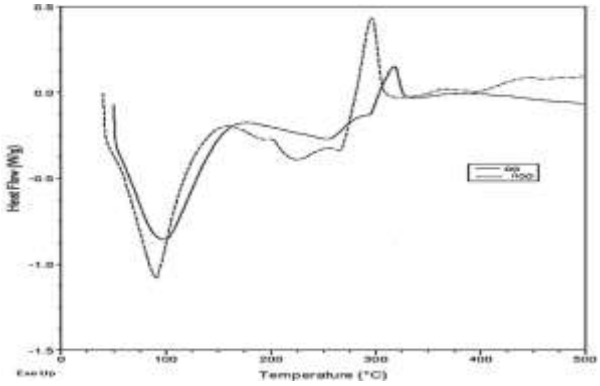

Figure5:-DifferentialScanningCalorimetryofGuar gum(GG) and Aminated guar gum(AGG).

The DSC thermogram of pure Ibuprofen showed a sharp endothermic peakat 100.00ºC which corresponds to its melting point.Observation revealed that the drug is pure without any impurities.SC thermogram shows the thermal behavior of native and aminated guar gum. For native guar gum, endothermic peaks were detected at 253 and 296 ◦C, and exothermic peak was detected at 317 ◦C. Aminated guar gum showed endothermic peaks at 223 and 274 ◦C, and exothermic peak at 295 ◦C. All endothermic and exothermic peaks for both guar gum samples are shown in the above figure.

Fourier TransformInfraredStudies
The FTIR Spectra of Ibuprofen in pure form and theirphysical mixturewas observed, the result showed that there is no interaction between drug andpolymers. From the FTIR spectral Figures 6 to 10 Interpretations the followingresult was obtained. The FTIR of Ibuprofen and combinations of polymers showsintense bandin thetable7 to 10asfollows.

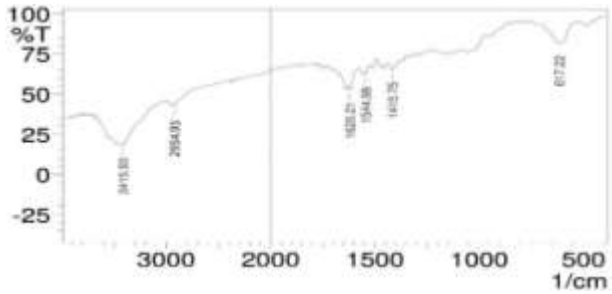

Figure 6:- FTIR Spectrum of Ibuprofen.

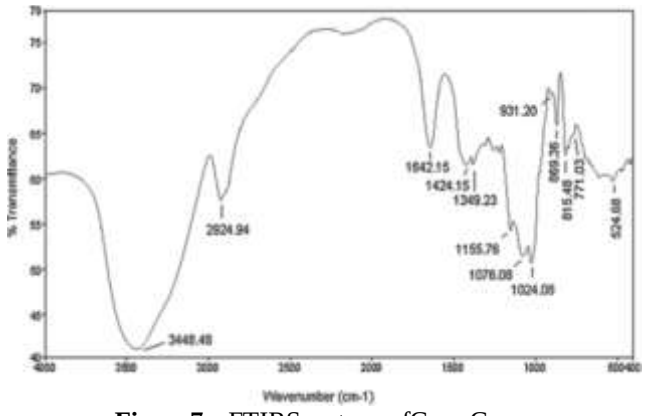

Figure7:- FTIRSpectrumofGuar Gum.

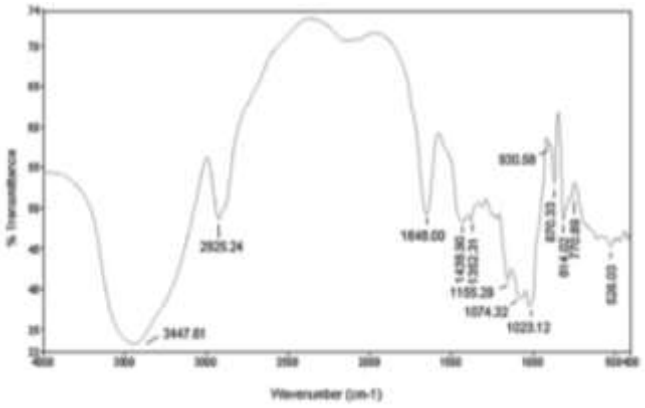

Figure 8:-FTIRSpectrumofIbuprofen+Guar gum.

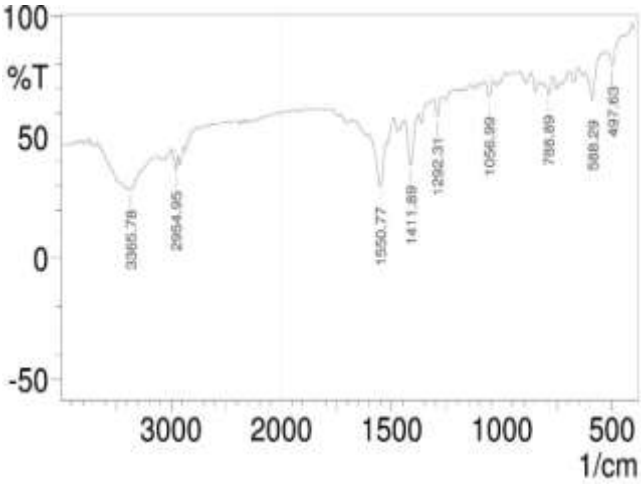

Figure 9:- FTIR Spectrum of Ibuprofen+ aminated Guar gum.

Powder X-ray diffraction (XRD)

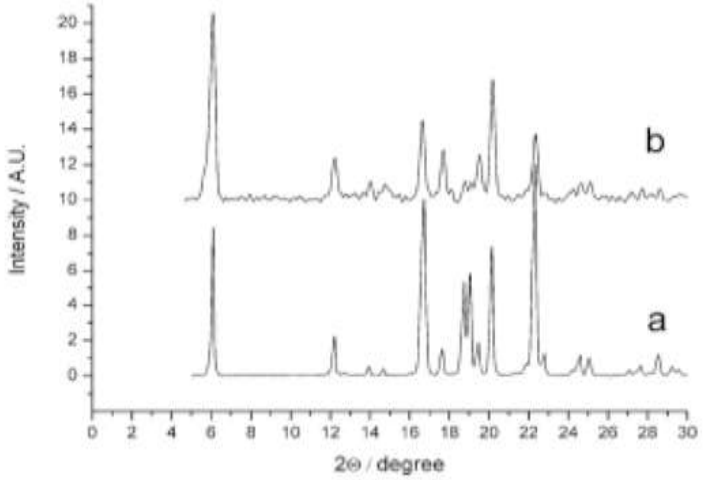

Figure 10:- XRD Graph Of a) Pure Ibuprofen and b) Ibuprofen in Optimized Formulation SD3.

The powder X-ray diffraction patterns of solid disperssions and original powder are compared in Figure 9. Both XRDpatterns from Solid disperssion and original substance correspond to racemic ibuprofen,that is, the Solid disperssion structure a similar precious stone stage as the first substance. The little distinction in the pinnacle

relative powers between thecurves a and b in the range of 17 < 2Θ < 21 is probably related to the difference in distribution of crystallographic orientations in the microsized original powder and Solid disperssion.

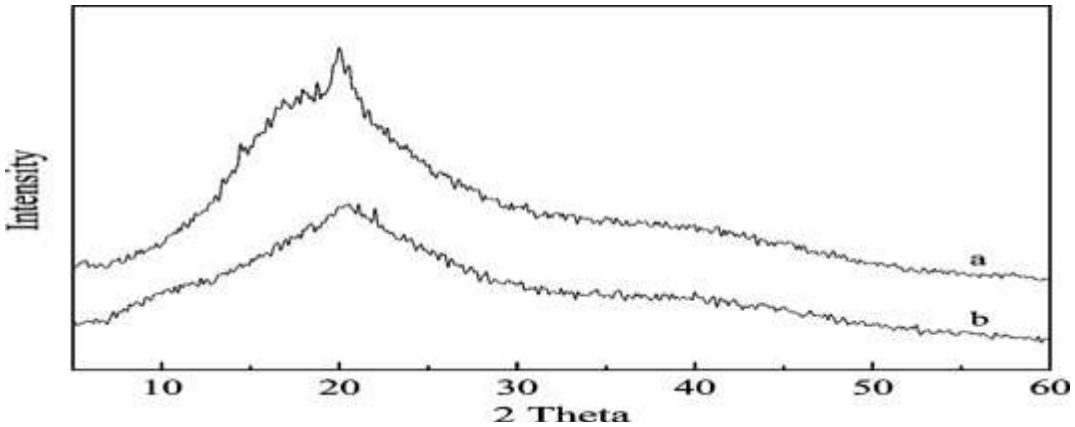

Figure 11:-XRD pattern of GG (a) and a representative AGG

The wide point X-beam diffractogram of local guar gum and an agent Aminated guar gum is introduced in Fig. 10. From Fig.10a, clearly local guar gum displays a tiny crystallinity. Comparable appearance has been accounted for local guar gum in the writing (Pal, Mal, and Singh, 2007). After Amination, an articulated decrease in crystallinity is noticed (Fig. 10b). This misfortune in crystallinity could be credited with the impact of the substitution of the Amine bunches by the Amination cycle. Amine bonds keep up with the dependability of guar gum gem, when they are broken, it could prompt diminishing the crystallinity.The drug content of each solid dispersion batch and physical mixture weredetermined byUV-spectrophotometrymeasured at 222nm.

Table 4:- Drug content of evaluation of solid dispersion containing Drug andCarriersfor various formulations.

Batchcode	%Drugcontent±S.D
S.D1	90±0.18
S.D2	95±0.78
S.D3	99±0.83
S.D4	91±0.74
S.D5	92±0.84
S.D6	93±0.74

Solubility Studies of Solid Disperssions of Ibuprofen

The solubility data of the physical mixtures containing Ibuprofen and guar gum, and Aminated Guar gum shown in Table 5. The solubility profile of the physical mixtures of Ibuprofen is shown infigure 12.

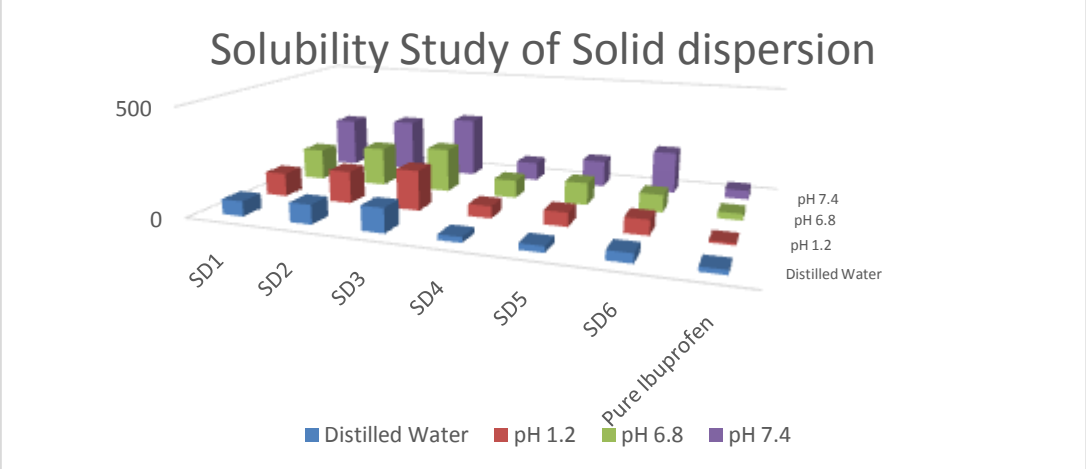

Figure 12 :-Solubility Studies of Solid Disperssions of Ibuprofen.

Table 5:- Solubility Studies of Solid Disperssions of Ibuprofen.

a) Formulation Code	b) Distilled Water	c) pH 1.2	d) pH 6.8	e) pH 7.4
f) SD1	g) 70±0.44	h) 110±0.60	i) 148±0.28	j) 234±0.20
k) SD2	l) 90±0.24	m) 150±0.60	n) 182±0.12	o) 250±0.92
p) SD3	q) 112±0.62	r) 186±0.36	s) 206±0.55	t) 284 ±0.86
u) SD4	v) 25±0.66	w) 56±0.97	x) 84±0.83	y) 88±0.83
z) SD5	aa)28±0.66	bb)64±0.24	cc) 104±0.28	dd)125±0.46
ee) SD6	ff) 42±0.61	gg)70±0.56	hh)82±0.38	ii) 196±0.84
jj) Pure Ibuprofen	kk) 20±0.49	ll) 10±0.86	mm)30±0.62	nn)42±0.24

As related to pure drug and, the solid dispersions prepared by Hot Melting Method showed higher solubility in Solid dispersions with Aminated Guar gum than the Solid Dispersions with Native Guar gum (Figure 12). The current examination proposed that this may be conceivable because of the planning of strong scatterings utilizing fluctuating convergences of normal transporters, which framed an eutectic combination and expanded the wettability of Ibuprofen and thus its solvency.

InvitrodrugreleasestudyofsoliddispersioncontainingDrugandcarriersfor variousformulations

Table 6:- InvitrodrugreleasestudyofsolidispersionontainingDrugandcarriersforvariousformulations.

Time(min)	CumulativePercentageofDrugReleased±std dev.						
	S.D1	S.D2	S.D3	S.D 4	S.D 5	S.D6	PI(Pure Ibuprofen)
0	0	0	0	0	0	0	0
5	10±0.11	13±0.15	12±0.13	10±0.16	10±0.11	12±0.12	0.005±0.32
10	12±0.12	22±0.37	20±0.32	23±0.22	20±0.54	24±0.45	1.009±0.03
15	16±0.24	30±0.22	23±0.63	31±0.34	28±0.22	29±0.27	3.024±0.21
20	20±0.14	40±0.68	30±0.24	52±0.18	35±0.33	32±0.36	4.043±0.052
25	27±0.23	52±0.35	36±0.16	70±0.16	46±0.56	38±0.24	7.19±0.35
30	33±0.88	60±0.54	48±0.34	74±0.14	50±0.38	46±0.28	10.361±0.42
35	38±0.54	67±0.18	52±0.25	79±0.18	63±0.13	56±0.44	11.54±0.07
40	42±0.82	70±0.17	67±0.23	84±0.20	68±0.26	64±0.83	11.892±0.09
45	50±0.24	72±0.19	78±0.26	88±0.23	74±0.16	73±0.56	13.892±0.12
50	63±0.56	80±0.17	80±0.48	90±0.18	84±0.22	86±0.38	15.892±0.26
55	72±0.58	86±0.19	92±0.16	93±0.27	89±0.43	90±0.22	18.892±0.32
60	80±0.88	90±0.38	98±0.32	96±0.30	93±0.26	95±0.32	20.892±0.71

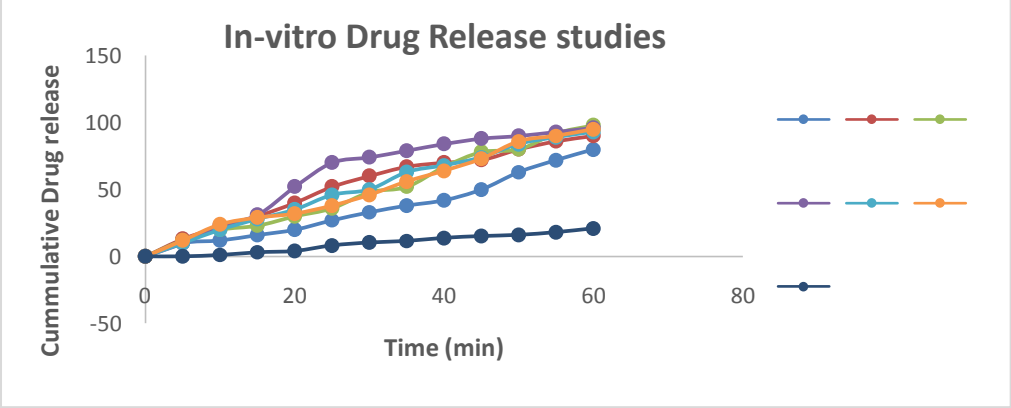

Figure 13:-In vitro drug release study of solid dispersion containing Drug and Carrier for various formulations

ThesoliddispersionofS.D3 batchshowedmaximumdrugcontent[99±0.83] and drug release [98%] and pure drug solution showed the most low release about 20% within 60 minutes, among all the formulationsand this ratio can be used to augment the solubility and dissolution rate of poorlywater soluble drug Ibuprofen. It was observed that the drug release was increasedwith increasingthequantityof Aminated Guar gum.

StabilityStudy
After storage the formulation was analysed for various parameters, resultsare showed in Table7.

Table 7:- StabilitystudyofbestformulationSD3.

Characteristic	Initial	10days	20 days	30 days	45 days
Appearance	White	Nochange	Nochange	Nochange	Nochange
Texture	Smooth	Smooth	Smooth	Smooth	Smooth
Drugcontent(%)	99.80±0.48	99.5±0.45	99.04±0.62	98.89±0.45	98.79±0.54
%of Drugrelease	97.41 ±0.16	97.23±0.34	96.45±0.22	96.24±0.43	96.01±0.42

Allthe values are expressedasmean±SD,n=3

From the table 7, there was no visible changes in the appearance of theformulation SD3and the drug content and dissolution profile of the optimizedformulationwasrelatedto theinitial reference.

Conclusion:-

The purpose of theexisting study was developed solid dispersion of NSAIDS like Ibuprofen by using functionalized guar gum. The results of FTIR study andDSC study confirmed that there is no chemical interaction or no incompatibilityamid the drug and excipients. The solid dispersion technique using Aminated guar gum would be aneffectiveapproachforincreasingthesolubilityandincreasingdissolutionbehaviourofpoorlywatersolubledrug than the native Guargum.

The *in vitro* dissolution study was performed for the prepared formulations. Based on the results SD3 was shown highest drug release99.41%within24hrs.

StabilitystudywasconductedasperICHguidelinesandtheresultsshowedthat there isno physicalor chemical change.

It may be concluded that the Solubility of Drugs Can be improved by using Funtionalized Guar gum in the Solid Dispersion, which provides a wide scope for the therapeutic efficiency.

Acknowledgement:-

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