RESEARCH ARTICLE

ROLE OF FUNCTIONALIZED GUAR GUM IN SOLID DISPERSION OF NON-STERoidal 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 ibuprofen. 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 incompatibility 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 particlesorcrystallineparticles. 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 particlesorcrystallineparticles.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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Natural carrier
More hydrophilic nature of carriers enhances the faster release of drugs from solid dispersion. A poor water soluble or insoluble carriers may lead to slower release of drugs.

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 the high 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 has been reported to improve the functional properties of native gums. Reports in the literature suggest that the derivatives of polysaccharides (amine, thiol, carboxymethyl) can be employed to manipulate swelling, bioadhesion and drug release. 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-rind kernel powder, aminated tamarind kernel polysaccharide, thiolated chitosan.

Materials and Methods:
Chemicals Used
Ibuprofen, Guar gum, Ethylene diamine, Sodium Bromide, Ethyl alcohol procured from Loba Chem. Mumbai, India.

Instruments Used
Analytical Balance (Shimadzu, Japan.), FTIR Spectrophotometer (Jasco FT-IR 8201PC), Dissolution Apparatus (Electro lab TDT-08L), Differential Scanning Calorimetry (PerkinElmer, Pyris 6 DSC, Germany), UV Spectrophotometer (U.V 1700 Shimadzu, Japan.) and Hotairoven (Thermolab)

Preformulation Studies
Construction of Standard Graph of Ibuprofen in pH 7.4 Phosphate buffer by using the UV method
100 mg of ibuprofen was weighed and transferred into a 100 ml of volumetric flask and was dissolved in phosphate buffer of pH 7.4 and make up to 100 ml. This was the standard stock solution containing 1 mg/ml of ibuprofen. From this stock arrangement, 10 ml was taken and made up to 100 ml with phosphate cushion pH 7.4. This was the second standard stock solution (100 μg/ml). From this solution, dilutions of 10 μg/ml, 20 μg/ml, 30 μg/ml, 40 μg/ml, 50 μg/ml were made and absorbance was measured at 222 nm.
Synthesis of Functionalized Guar gum

Amination of Guar gum

In 3000ml water add 60gm of Natural Guar gum. To this solution add aminating agent ethylene diamine (25ml) with continuous stirring at constant temperature (20-60°C) for 6 hr. then slowly add reducing agent Sodium Bromide (NaBH₄) 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.

PreFormulation Studies

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.

Differential Scanning Calorimetry (DSC)

The differential scanning calorimetry (DSC) of pure drugs, solid dispersion, and the physical mixture of the remedy was performed using the DSC instrument (Perkin Elmer Pyris 6 DSC, Germany), for the measurement of heat loss 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 30°C and afterward a steady warming pace of 10°C/min was utilized something like 400°C under nitrogen temperature.

Fourier Transform Infrared (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 1 cm⁻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-ray 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.

Formulation Development

Preparation Solid dispersion of Ibuprofen

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

Preparation of physical mixture containing Ibuprofen

The corporeal assortments of Ibuprofen-guar gum and Ibuprofen Aminated guar gum in the identical heft ratio (1:3) were primed by scrupulously mixing the appropriate amount of two components for 10 min in a mortar. The concoctions were sieved through a 60 mesh screen and stored in a desiccator for further evaluation. Solid dispersions were prepared by hot melt method. Corresponding physical mixtures were heated in an oil bath at 175°C until they melted.
Solidification was reached by cooling to room temperature under ambient conditions. Afterwards, the mixture was pulvérised, sieved, and the fraction ≤160µm was selected. The method of preparation and composition were given Table 1.

Table 1: Composition of various batches of Physical mixtures and Ibuprofen Solid Dispersion.

| Batch Code | 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   |

Evaluation of Ibuprofen solid dispersions and corporeal mixtures

Evaluation studies were carried out by estimating drug content and invitro dissolution studies.

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.

Drug content

The drug content of each solid dispersion physical mixture were determined by UV-spectrophotometry. Accurately weighed quantity of samples from all batches equivalent to 100 mg of Ibuprofen was transferred to a 100 mL volumetric flask containing 100 mL of phosphate buffer pH 7.4 and the absorbance was measured at 222 nm.

Invitro dissolution studies

The prepared solid dispersions were accurately weight equivalent to 100 mg of the drug. These solid dispersions are filled in empty capsules and analysed for drug release in 900 mL of phosphate buffer pH (7.4) as dissolution medium at 37±0.5°C and 50 rpm. 5 ml of the sample solution was taken from the dissolution apparatus and the same volume replaced with fresh dissolution medium at predetermined time intervals for 5 min. The absorbance of these solutions was measured at 222 nm using UV-Vis spectrophotometer.

Stability studies

Stability study was carried out to observe the effect of temperature and relative humidity on selected formulation (SD3), by keeping at 40±2°C, in air tight high density polyethylene bottles for six months, at RH 75±5%. Physico evaluation was carried out in each month.

Table 2: ICH guidelines for Stability study.

| Study      | Storage condition                  | Timeperiod |
|------------|------------------------------------|------------|
| Longterm   | 25°C±2°C/60%RH±5%RH                | 12 month   |
| Intermediate | 30°C±2°C/65%RH±5%RH               | 6 month    |
| Accelerated | 40°C±2°C/75%RH±5%RH               | month 6    |

Results and Discussion:-

Preparation of Calibration curve for Ibuprofen

Table 3: Calibration curve of Ibuprofen.

| Concentration(µg/ml) | Absorbance(222nm) |
|----------------------|-------------------|
| 0                    | 0                 |
| 10                   | 0.151             |
| 20                   | 0.351             |
| 30                   | 0.521             |
| 40                   | 0.713             |
| 50                   | 0.912             |
The calibration curves were linear and obeyed Beer-Lambert’s law in the concentration range 10-50μg/ml. The correlation coefficient values were 0.9986 indicating excellent linearity of the data.

**Appearance**
Ibuprofen appeared as crystalline solid.

**Melting point**
Melting point of drug was determined by capillary method. The result is found to be 75-77°C.

**Saturation solubility**

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 to enhance its solubility.
Compatibility Studies
Differential Scanning Calorimetry (DSC)

Figure 4: Differential Scanning Calorimetry of Ibuprofen

The DSC thermogram of pure Ibuprofen showed a sharp endothermic peak at 100.00°C 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 Transform Infrared Studies

The FTIR Spectra of Ibuprofen in pure form and their physical mixture was observed, the result showed that there is no interaction between drug and polymers. From the FTIR spectral Figures 6 to 10 interpretations the following result was obtained. The FTIR spectra of Ibuprofen and combinations of polymers shows intense band in the table 7 to 10 as follows.

Figure 5: Differential Scanning Calorimetry of Guar gum (GG) and Aminated guar gum (AGG).

Figure 6: FTIR Spectrum of Ibuprofen.

Figure 7: FTIR Spectrum of Guar Gum.
Figure 8: FTIR Spectrum of Ibuprofen + 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 dispersions and original powder are compared in Figure 9. Both XRD patterns from Solid dispersion and original substance correspond to racemic ibuprofen, that is, the Solid dispersion structure is similar to the previous state as the first substance. The little distinction in the pinnacle
relative powers between the curves a and b in the range of \(17 < 2\theta < 21\) is probably related to the difference in distribution of crystallographic orientations in the microsized original powder and Solid dispersion.

![XRD pattern of GG (a) and a representative AGG](image)

**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 were determined by UV-spectrophotometry measured at 222nm.

**Table 4:** Drug content of evaluation of solid dispersion containing Drug and Carriers for various formulations.

| Batchcode | %Drug content±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 Dispersions 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 in Figure 12.

![Solubility Study of Solid dispersion](image)

**Figure 12:** Solubility Studies of Solid Dispersions of Ibuprofen.
Table 5: Solubility Studies of Solid Dispersions of Ibuprofen.

| a) Formulation Code | b) Soluble in Water | c) pH 1.2 | d) pH 6.8 | e) pH 7.4 |
|---------------------|---------------------|-----------|-----------|-----------|
| f) SD1              | 70 ± 0.44           | 110 ± 0.60| 148 ± 0.28| 234 ± 0.20|
| k) SD2              | 90 ± 0.24           | 150 ± 0.60| 182 ± 0.12| 250 ± 0.92|
| p) SD3              | 112 ± 0.62          | 186 ± 0.36| 206 ± 0.55| 284 ± 0.86|
| u) SD4              | 25 ± 0.66           | 56 ± 0.97 | 84 ± 0.83 | 88 ± 0.83 |
| z) SD5              | 28 ± 0.66           | 64 ± 0.24 | 104 ± 0.28| 125 ± 0.46|
| ee) SD6             | 42 ± 0.61           | 70 ± 0.56 | 82 ± 0.38 | 196 ± 0.84|
| jj) Pure            | 20 ± 0.49           | 10 ± 0.86 | 30 ± 0.62 | 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.

Invitro drug release study of solid dispersion containing Drug and carriers for various formulations

Table 6: Invitro drug release study of solid dispersion containing Drug and carriers for various formulations.

| Time (min) | S.D1 Cumulative Percentage of Drug Released ± std dev. | S.D2 Cumulative Percentage of Drug Released ± std dev. | S.D3 Cumulative Percentage of Drug Released ± std dev. | S.D4 Cumulative Percentage of Drug Released ± std dev. | S.D5 Cumulative Percentage of Drug Released ± std dev. | S.D6 Cumulative Percentage of Drug Released ± std dev. | Pl (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 formulations and this ratio can be used to augment the solubility and dissolution rate of poorly water soluble drug Ibuprofen. It was observed that the drug release was increased with increasing the quantity of Aminated Guar gum.

Stability Study
After storage the formulation was analysed for various parameters, results are showed in Table 7.

Table 7:- Stability study of best formulation SD3.

| Characteristic       | Initial     | 10 days     | 20 days     | 30 days     | 45 days     |
|----------------------|-------------|-------------|-------------|-------------|-------------|
| Appearance           | White       | No change   | No change   | No change   | No change   |
| Texture              | Smooth      | Smooth      | Smooth      | Smooth      | Smooth      |
| Drug content (%)     | 99.80±0.48  | 99.5±0.45   | 99.04±0.62  | 98.89±0.45  | 98.79±0.54  |
| % of Drug release    | 97.41±0.16  | 97.23±0.34  | 96.45±0.22  | 96.24±0.43  | 96.01±0.42  |

All the values are expressed as mean±SD, n=3

From the table 7, there was no visible changes in the appearance of the formulation SD3 and the drug content and dissolution profile of the optimized formulation was related to the initial reference.

Conclusion:-
The purpose of the existing study was developed solid dispersion of NSAIDS like Ibuprofen by using functionalized guar gum. The results of FTIR study and DSC study confirmed that there is no chemical interaction or no incompatibility amid the drug and excipients. The solid dispersion technique using Aminated guar gum would be an effective approach for increasing the solubility and increasing dissolution behaviour of poorly water soluble drug than the native Guar gum.

The in vitro dissolution study was performed for the prepared formulations. Based on the results SD3 was shown highest drug release 99.41% within 24 hrs.

Stability study was conducted as per ICH guidelines and the results showed that there was no physical or chemical change.

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

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