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ENHANCEMENT OF DISSOLUTION RATE OF IBUPROFEN BY USING POLYMERS

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Abstract: We use different types of solubilisers like PVP K 30, PEG 400, and Tween 80 for increasing solubility of ibuprofen. In case of solubility we use combined effects of that polymers is use to easy to enhancement the solubility as well as activity of ibuprofen by using solid dispersion technique. In case of solid dispersion we use carrier such as Poly ethylene Glycol, Poly ethylene Glycol and polyvinyl pyrrolidone for dissolution study using USP type of paddle method is used. Solid dispersion method shows by using different types of polymers we can increase the solubility of ibuprofen. The tablet manufactured by solid dispersion techniques it gives better dissolution profile than common tablet and also most used in case of pH changes in particular manner. It is also used in the solution containing ibuprofen in some conditions we required to dissolve tablet in different pH that conditions this method is most useful.

Keywords: Solubility, solid dispersion, PVP K-30, Tween-80, PEG-4000, Polyethylene glycol (PEG), Polyvinylpyrrolidone (PVP) Polyvinyl alcohol (PVA), Crospovidone (PVPCL), Polyvinylpyrrolidone polyvinyl acetate copolymer (PVP-PVA) etc.

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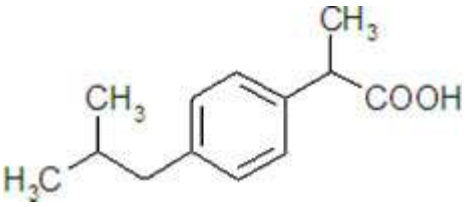
INTRODUCTION

Ibuprofen is most potent orally active non steroidal anti-inflammatory drugs used for different treatment of acute and chronic pain. It having better tolerated than other NSAIDs then we study at evaluating some quality control parameters to compare the quality, safety, and efficacy of ibuprofen tablets available in the Indian market.

STRUCTURE OF IBUPROFEN: -



Chemical name: - (RS)-2-(4-Isobutylphenyl) propionic acid

THERAPEUTIC CRITERIA AND INDICATIONS: -

Ibuprofen is a mostly used as nonsteroidal anti-inflammatory drug (NSAID) having racemic compound have great regard of a nonselective (COX)-inhibitor i.e. cyclooxygenase and the S (þ) -enantiomer was found to be a selective COX-1 inhibitor while R -ibuprofen has little Pharmacodynamic effect. The racemic ibuprofen and enantiomer are mainly used in the treatment of moderate pain related to migraine, headache, and dental pain and some other diseases depending upon that the solubility of compound is very important role in dissolution study so following are the solubility values of ibuprofen.

Table1. Solubility Data at 20°C and 37°C (mg/mL) and Dose/Solubility Ratio's at 37°C (mL) of Two Strengths of Ibuprofen

	20°C			37°C		
				Dose/solubility ratio		
pH	Higgins et al.7	Stippler8	Calculated7	Experimental	For 400 mg	For 800 mg
1	<0.1	-	0.027	0.038	10526	21053
1.2	-	0.037	-	-	-	-
2	-	-	-	-	-	-

3	<0.1	-	0.027	-	-	-
4	<0.1	-	0.028	0.043	9302	1860.5
4.5	-	-	0.037	-	-	-
5	-	-	-	0.084	4762	954
5.5	-	0.0894	0.13	-	-	-
6	1.0	-	-	-	-	-
6.8	-	-	-	0.685	58	1168
7	-	2.472	1.1	3.37	119	237
7.2	-	-	10	-	-	-
7.4	-	4.52	-	3.44	-	-
8	>100	-	80	-	116	233

The dose and solubility parameter outside the difficult limit of <250 ml.

In the text only data at 20°C or room temperature were found. BCS categorization requires facts on the solubility at 37°C, these morals were experimentally determined, intended for each medium in triplicate. Ibuprofen drug material was suspended in medium and stirred for 24 h at 37°C and then stored for a further 24 h without disturbance. In every case residue on the bed of the flask was observed. The ibuprofen concentration in the apparent supernatant was determined by UV-analysis. These outcomes are also exposed in Table 1 reported a minimum solubility at pH 2.0. Conversely, such a negligible was not re-ported with other employees and is not in traditional values with the molecular structure. The individual R and S isomers have better solubility at pH 1.5 (9.5 mg/100 ml) than the racemate (4.6 mg/100 ml) Complexation with b-cyclodextrin resulted in enhanced wettability and immediate termination. Polymorphism Ibuprofen does not exhibit genuine polymorphism. However, it has a affinity towards slight crystal trellis adjustment, which may affect also its dissolution performance.

PARAMETERS WHICH USED IN PROGRESS THE ACTION OF IBUPROFEN:

POLYMORPHISM:

Ibuprofens do not demonstrate genuine polymorphism. However, it has an affinity towards minor crystal lattice adjustment, which may affect also its dissolution behavior.

PARTITION COEFFICIENT:

To estimate of the n-octanol-water distribution coefficient gave log D values of 3.7, 3.6, 2.1, and 1.2 at pH values of 1, 4, 6, and 7, correspondingly. Other employee's predictable log P (n-octanol/water) and Clog p values of 3.68 and 3.14, correspondingly, using different methods based on tiny donations to lipophilicity, whereas for the greatly permeable marker drug Metoprolol, using the similar methodology, log P and Clog p values of 1.72 and 1.35 were calculated.

pKa:-

The pKa of ibuprofen is in the sequence of 4.5–4.6. And the dose potency of Marketed medicine Products Strengths of IR solid oral dosage form with a marketing agreement (MA) in Germany (DE) range from 200 to 800 mg. The WHO List of important Medicines includes strengths of 200 and 400 mg.

ABSORPTION AND PERMEABILITY:

Following oral administration of ibuprofen, highest plasma concentrations are reached within 1–2 h in humans with an unqualified bioavailability (BA) of about 100%. Antacids like magnesium hydroxide gather speed the rate of absorption suitable to pH changes in the GIT system induced by the antacid. Also, ibuprofen absorption was greatly slower when concomitantly administered with aluminum hydroxide medicine like capsules than with sodium Bicarbonate medicine like capsules. A grade order relationship was observed connecting dissolution parameters and the in vivo outcome that reflect rate of absorption, Food drinking also affects the absorption rate of ibuprofen, which is possible due to food induced pH altitude in the stomach consequential in earlier in vivo dissolution of ibuprofen. Rapid and entire absorption suggests a high permeability through the GI covering.

PHARMACOKINETICS:

Linear pharmacokinetics of ibuprofen has be report in the dose series of 200–400 mg. At doses superior than 400 mg nonlinearity has be reported, but this is more possible due to changes of plasma protein binding than abridged absorption. Dose linearity in the absorption of S(þ)-ibuprofen inside the dose range of 200–600 mg has as well been documented. Ibuprofen is expansively spring and bound to plasma proteins. Ibuprofen undergoes universal unidirectional inversion to S(þ)-ibuprofen, which is identified to be the main pharmacodynamically energetic moiety.

DOSAGE FORM PERFORMANCE:

The pharmacokinetic properties of one or two ibuprofen provision were compared in a randomized intersect learn on ten strong volunteers; there was no statistically important differentiation in the extent of absorption however ibuprofen peak plasma concentrations differ between the one two preparations. The authority of incorporation of a variety of different obligatory agents on the in vitro rate of dissolution the ibuprofen formulations was investigate by (Ghosh et al)., using a different type rotating basket. As termination media, 0.1 and 0.1N HCl contain a variety of concentrations of sodium laurylsulphate be used and Polyvinylpovidone-containing preparation formulations show the greatest in vitro dissolution, but no assenting pharmacokinetic study be carried out. In an additional study, the pharmacokinetic parameter and properties of a soft gelatin capsule along with a film coated tablet be compared to those obtain after the management of liquid prepared from bubbling tablets.

DISSOLUTION STUDAY:-

The present USP 27 requirement for in vitro dissolution requires NLT 80% dissolved within 60 min having capacity of paddle apparatus was 900 ml. It contains phosphate buffer having pH 7.2 at 50 rpm. A bulky number of IR remedy products marketed in DE showed additional rapid dissolution, using a confrontation speed of 75 rpm on the same pH, while difference designed for some products were at a standstill obvious. Under individuals test conditions, approximately all medicine products met the criterion for speedy dissolution as definite in BCS guidance's, that is, 85% within 30 min.

SOLUBILITY OF IBUPROFEN:

The numerous reports going on the solubility at 20°C are in logical agreement among each other and also maintain our investigational values at 37°C, being to some extent higher than the values at 20°C, as be able to be expected. Solubility for biowaiver purposes should be resolute at 37°C and at with the purpose of temperature, at pH values lower pH 5.5 their dose/solubility fraction exceeds the significant value of 250 ml for equally strengths considered. So, ibuprofen is unsolvable in acid and accordingly not ''highly soluble'' as definite according to the current BCS guidance's.

ABSORPTION AND PERMEABILITY:

The Bioavailability of about 100% previously classify ibuprofen as ''greatly permeable'' according near the present BCS Guidance's. This categorization is support from mutually in vivo as well as in vitro data. Assimilation and absorption of ibuprofen occur all through the GIT tract. A Paddle apparatus exceeding 10_10_6 cm/s is considered to involve elevated and high

permeability. The results report since Caco-2 studies beat this value, in line with the higher Paddle apparatus found for ibuprofen than for propranolol; propranolol is suggested as a high permeability suggestion substance used for Caco-2 permeability in the FDA guideline.

FOLLOWING MAJOR ANNOUNCEMENT FOR IMPROVEMENT SOLUBILITY OF IBUPROFEN:

Chemistry moved as of wet chemistry to combinatorial chemistry with high throughput Viewing which resulted into anamplify of badly water soluble drugs. In this example, approximately 70% of new drug candidate comprise shown poor aqueous solubility in drug discovery with its relative application currently, approximately 40% of the market instant release (IR) oral drugs be categorize as nearly unsolvable. The aqueous solubility of a medicine is a critical and much determinant of its dissolution rate and consequently oral bioavailability of orally administer drug it can be overcome problem of poor aqueous solubility various approach have been investigate in drug development and growth of research. Modification in solubility can be achieved on two levels, while chemical modification of the drug particle or though scheming of formulation which is as well referred as physical modification. The development of solubility and dissolution profile of these lipophilicity medicine and drug partials or molecules with no altering the molecular structure is a meticulous confront for formulation scientist.

DEVELOPED METHODS FOR SOLID DISPERSION:

A variety of manufacturing methods are used for preparation and formulation of solid dispersion widely used two methods that fusion method and solvent evaporation method.

FUSION METHOD:

The Sekiguchi and Obi primary reported melting or fusion method designed for SD of drug contain urea as a carrier. In this method, drug or medicine and carrier is heated and high warmed till it melting, followed by cooling and solidification with the use of ice-bath confrontation, stainless steel slim layer distribution followed by a cold drought, put on plates placed over dry ice with maintain cool atmosphere, immersion in liquid nitrogen, on top of Petridis inside desiccators. Lastly, solid mass is crushed with help of muster and pastel, pulverized and sieved for better handling. However, Heat sensitive or thermo labile drugs cannot be process at high heating temperature and degradation of those drugs with even carrier is main limitation of fusion procedure. At molten stage, thickness and viscosity of polymeric carrier may be elevated which cause improper addition of medicine or drug and carrier. To conquer the limitations of fusion method modified technique like hot stage extrusion or melt agglomeration be incorporated in fusion method.

SOLVENT DEPARTURE AND EVAPORATION METHOD:

The solvent evaporation method was primary used by Tachibani and Nakumara in which both the drug and the delivery service were dissolved in an ordinary solvent and then the solvent was evaporate under vacuum to create a solid solution. In this method, the thermal dilapidation of drugs and/or carriers can be minimized, since disappearance of organic solvent occurs at less temperature. Selection of a general solvent for both drug and carrier may be grave, and residual solvent in the product may create dogmatic issues. Various process are used for evaporation of solvent similar to freeze-drying, spray-drying, vacuum drying, the use of supercritical fluids , the utilize of a rotary evaporator, heat of the mixture on a hot plate, etc.

CARRIERS USED IN SOLID DIFFUSION:

While selecting a carrier for solid diffusion of drug more than a few factors need to be careful. The majority important factors are the scenery of carrier, drug to carrier percentage, method of preparation, polymer series length/molecular mass and synergistic outcome of two carriers.

DESCRIPTION OF SOLID DIFFUSION:

Solid diffusion can be characterized with numerous methodical methods. FT-IR Spectroscopy, scanning electron microscopy, X-ray diffraction, termination rate fortitude and thermal analysis methods like thermo-microscopic method, degree of difference thermal analysis (DTA), and degree of difference scanning colorimetric (DSC) can be working for solid dispersion assessment.

RESULT & DISCUSSSION

The research report on formulation development solubility of drugs is widely encounter problem which leads to low bioavailability and higher therapeutic dose **was prepared & studied.** Extensive choice for carriers makes solid dispersion a very versatile tool for drug development. Proper selection of carrier and manufacturing method are vital parameters for successful formulation of solid dispersion and lastly this polymer and solid dispersion method use to enhance the ibuprofen solubility which are used in different types of formulations.

CONCLUSION

In the current time of formulation development solubility of drugs is widely encounter problem which leads to low bioavailability and higher therapeutic dose. Solid dispersion is one of the most attractive approaches to improve solubility of poorly soluble drugs. Development of solid dispersion region evolved from crystalline carrier in first generation to apply of surfactants in third generation with improvement in stability and performance.

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