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ORIGINAL ARTICLE

PREPARATION AND EVALUATION OF IBUPROFEN NANOSUSPENSION FOR SOLUBILITY ENHANCEMENT

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Abstract

Background: Ibuprofen is a nonsteroidal anti-inflammatory drug (NSAID) having poor water solubility and high permeability. The study aimed to prepare, characterize, and evaluate ibuprofen nanosuspensions to enhance its solubility and dissolution rate.

Materials & Methods: This was an experimental and laboratory-based study. Nanosuspensions of ibuprofen were formulated using three different polymers-PVP K30, Poloxamer 188, and HPMC E50-at various drug-to-polymer ratios (1:1, 1:2, 1:3). The study was conducted in a controlled laboratory environment, typically in a pharmaceutical or chemical research laboratory equipped with instruments like particle size analyzers, scanning electron microscopes, and dissolution apparatus. The formulation and characterization experiments were performed in compliance with standard protocols for nanoparticle formulation and pharmaceutical analysis

Results: All ibuprofen nanosuspensions were within the nano size range (123-564.5 nm), with the smallest particle size (123 nm) observed for PVP K30 at a 1:1 ratio. The PDI ranged from 0.008 to 0.071, and the specific surface area (SSA) ranged from 18.6 to 3.39 m^2/g. Saturated solubility of ibuprofen increased by approximately six-fold compared to the pure drug. Entrapment efficiency ranged from 85% to 97%, while the dissolution rate showed a significant improvement, with 98% of the drug released within 15 minutes, compared to 25% release from pure ibuprofen in the same period.

Conclusion: The solvent- Anti-solvent technique is effective for producing ibuprofen Nano-suspensions, significantly enhancing the solubility and dissolution rate of the drug. This formulation approach holds promise for improving the bioavailability of poorly water-soluble drugs like ibuprofen.

KEY WORDS: Dissolution rate; Ibuprofen; NSAID; Nanosuspensions; Polymers; Solvent anti-solvent technique.

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INTRODUCTION

Nanotechnology is a sub-division of science, which deals with study the material at molecular level on nano size range 10^{-9}m.[1] Nanotechnology has many advantage as compare with other traditional dosage form, some of these properties like a good effectiveness, dose reduction, management in drug delivery, protect the active ingredient from external environment, enhance bio distribution and lowering in toxicity and targeting.[2] Nanotechnology has a lot of applications in different pharmaceutical fields like preparation of liposome, nano emulsion, nanosuspension nanogel.[3] The solubility and dissolution are a rate limiting step for drug absorption from gastrointestinal tract and as well as therapeutic effectiveness of active ingredient.[4-7] One of the solution for poor water solubility of drug is using a technique of nanotechnology, by reduction in particle size.[8-11] Also, physical modification can be used like micronizing[12], solid dispersion[13,14] spray drying[15], solvent precipitation[16] and complexation[17] these techniques were used to reduce particle size with improvement in drug solubility of poor water soluble drug.[18]

Ibuprofen (IBU) is a nonselective COX inhibitor, nonsteroidal anti-inflammatory drug NSAID act as analgesic, potent pyrolysis and anti-inflammation is

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used an oral or rectal.[19-21] Ibuprofen belong to class II drug (BCS) according to the Biopharmaceutical Classification System. Ibuprofen has poor water solubility (21mg/L) at 25 C^0 and poor in gastro intestinal absorption[22], with serum half-life 1.8-2 hr. so it is rapidly bio transformed and patient need to repeate/ administer the daily dose 3-5 times.[23] Aim of the study was formulation and evaluation of Ibuprofen nanosuspension for solubility and dissolution rate enhancement. The physiochemical characterization of nanosuspension were done for particle size measurement, PDI, SEM and in vitro drug release.

MATERIAL AND METHOD

Ibuprofen was purchased from Lisihui naming chemical from MACLAN company, china, PVP k30, HPMC E50 and poloxamer 188 from Alpha Chemika India. Methanol was supplied from Romil UK, dihydrogen disodium hydrogen phosphate was obtained from Spine-Chem Limited. Shake flask method was used to determine the saturated solubility of Ibuprofen in distilled water. Ibuprofen Nano suspension formulas were prepared by using solvent anti solvent precipitation method. Ibuprofen was dissolved in methanol to prepare organic phase, while aqueous phase consists of different types of stabilizers in water. The organic phase was dropped drop by drop by using syringe on aqueous phase that contain stabilizer. The mixture of drug solution and stabilizer was allowed to stirred on magnetic stirrer for one hr. to evaporate of organic phase.[24,25] "Generation of nucleation and growth of particles by condensation which lead to aggregation of particles in a case of uncontrolled growth may be occur,[26] Ibuprofen is poor water soluble therefore was precipitated with stabilizer as a fine particle. The procedure was repeated by using various type of stabilizer with different drug to stabilizer ratio (1:1, 1:2, and 1:3) to produce different formulas of Ibuprofen nanoparticles, as show in table(1)

Table 1: Different Ibuprofen nanosuspension formulas with different type of stabilizer and different ratio

Formula No.	Ibuprofen mg	HPMC E50 mg	PVP k30 mg	Poloxamer 188 mg
F1	100	100		
F2	100	200		
F3	100	300		
F4	100		100	
F5	100		200	
F6	100		300	
F7	100			100
F8	100			200
F9	100			300

The size of particles and specific surface area was measure by using dynamic light scattering using ABTA-9000 Nano laser particle size analyzer, act by measure light scattering by molecules of the sample, at scatter angle 90^0 with constant temperature at $25C^0$ devoid of dilution of sample. Fresh prepare formula of Nano suspension was centrifuge at 15000 prm for 30 min. at temperature $4C^0$ by using cooling centrifuge. After separation take the supernatant and detected the concentration of free drug at nm using UV-spectrophotometric. EE was measured by subtract the weight of drug that found in the layer of supernatant from initial amount of drug in the formula. The experiment for each formula was repetitive triplicate.

$$\text{Entrapment Efficiency (\%)} = \frac{\text{Weight}_{\text{initial drug}} - \text{Weight}_{\text{free drug}}}{\text{Weight}_{\text{initial drug}}} \times 100\%$$

To determinate the shape and surface topography of particles, INSPECT S50 was used, the sample mounted on double side tape carbon in which coated with gold.[27] The release of drug was determined by using paddle dissolution apparatus. The dissolution performed by taking 100mg of Ibuprofen as a suspension and put directly to the dissolution media. The dissolution media in which consist from 900ml media of Ph 1.2 of 0.1N HCL and the temperature maintain at $37C^0$ and 50 rpm. At specific time interval 5ml of sample withdrawal at (5,10,15,20,30,40,50 and 60min.) follow that filter using 0.45 and analyze at using UV spectroscopy. Fresh media was added to maintenance the volume constant. Pure drug of Ibuprofen was used for compare.

RESULTS

Particle size of all formulas of Ibuprofen nanoparticle was within nano size range (123-564.5nm), the formula F4 smallest one (123nm) for pvpk30 at (1:1), while F3 the largest one (564.5nm) for HPMC E50(1:3), the PDI for all formula range from (0.008-0.071), mean all formula monodisperse distribution with a good physical stability. While SSA range from (3.39-18.6 m^2\g) The result of particle size as show in table 2. the formula F4 with (Ibuprofen: PVP k30 at ratio 1:1) show the smallest particle size and large surface area.

The effect the concentration of polymers for HPMC E50, as increase conc. will increase in particle size and when reach to ratio 1:3 show increase in particle size with a mean ratio of 1:1 is optimum conc. (F1-F3), and also PVPk30 (F4-F6) as increase concentration of polymer lead to increase in particle size, so the ratio 1:1 0f (Ibuprofen: PVP k30) is an optimum concentration and for poloxamer 188 (F7-F9) as increase in polymer conc. as show in figure (1)

Table 2: particle size, PDI and SSA for Ibuprofen nanosuspension formulas

Formula No.	Particle size nm	PDI	SSAm^2\g
F1	301.5	0.008	7.15
F2	503	0.071	3.39
F3	564.5	0.017	3.91
F4	123	0.011	18.6
F5	380	0.021	6.1
F6	399	0.012	6.13
F7	282.5	0.01	7.91
F8	252	0.009	8.8
F9	151	0.01	16.8

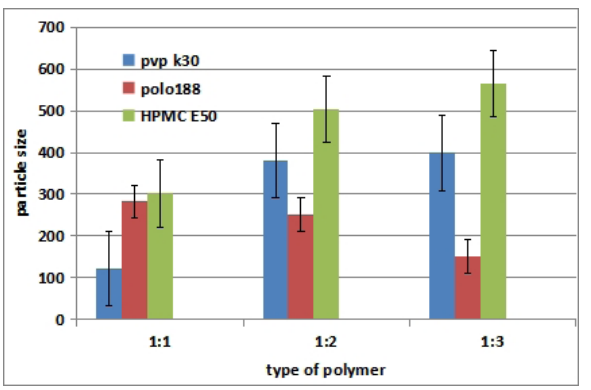

Figure (1): effect the type and concentration of stabilizer on particle size of Nano suspension

Entrapment efficiency can be measured as amount of drug that is present in nanosuspension to the amount of drug present initially, EE of the formulas of Ibuprofen nanosuspension range from 85% to 97%, which mean suitability of both polymers used and the antisolvent technique in preparation of Ibuprofen nanosuspension, as show in figure (2)

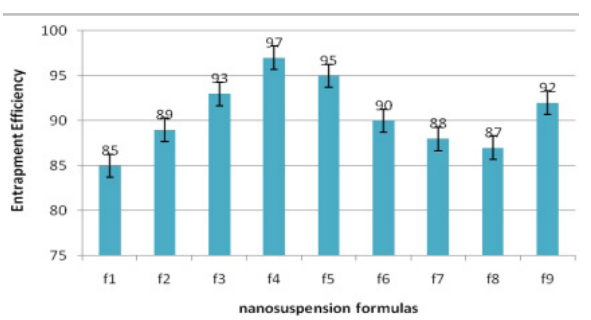

Figure 2: Entrapment efficiency of Ibuprofen nanosuspension

Scan electron microscope type INSPECT S50 was use to detected the surface morphology of Ibuprofen nano suspension, the picture shows a spherical particle with no aggregation, as expression in figure (3)

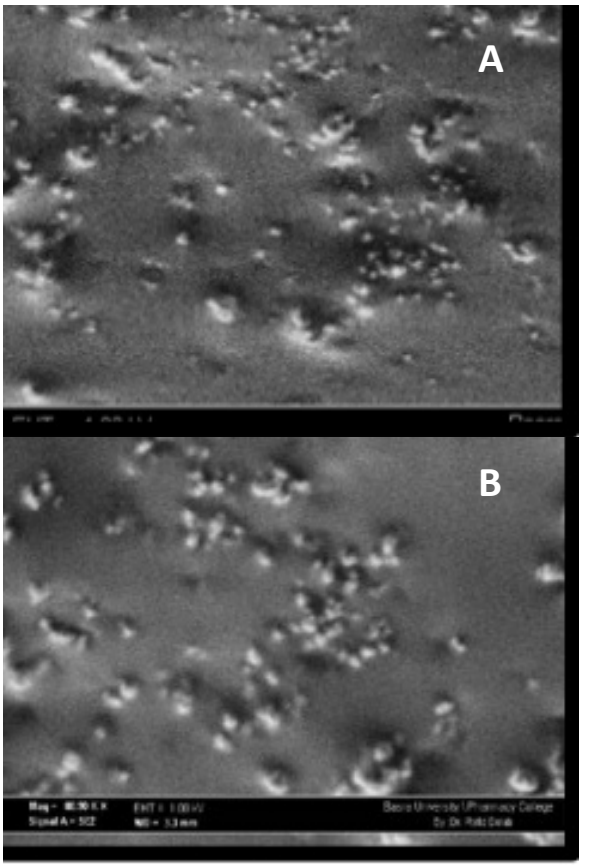

Figure (3): SEM for F4, A:88.90 KX magnifications, B:12.85 K X magnifications

In vitro dissolution rate was determined for pure Ibuprofen and the best formula(F4), the result show that at time 15 min 98% of drug release of formula F4 while only 25% of pure Ibuprofen, as seen in figure (4).

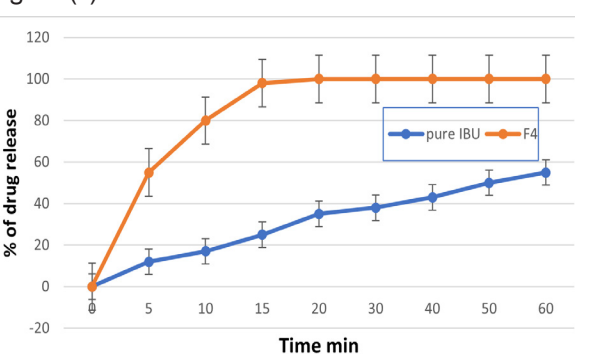

Figure (4): Drug release study of F4 and pure Ibuprofen (IBU) in 0.1N HCl (pH 1.2)

DISCUSSION

To study effect of type and concentration of polymers, different type of polymer (HPMC E50, PVPk30and

poloxamer188) with using various ratio of drug: stabilizer (1:1,1:2 and 1:3) for formulas (F1-F9). PVP k30 it's a non-ionic surfactant in which act by steric stabilizer, act by adsorb on the surface of particles through anchor segment and also act as wetting agent., which have amphiphilic part extend to bulk medium, and provide a physical stability by provide a coverage to new particles formed.[28] HPMC also act as steric stabilization which has a alkyl moiety show a good affinity to hydrophobic part of Ibuprofen.

Saturated solubility was determined for both pure Ibuprofen and the best formula F4 in water by using flask shaking method, the result show the solubility of pure Ibuprofen 21.5mg/L, while the solubility of the best formula F4 was 129.6mg/L approximately six fold increase in saturated solubility, as decrement in the size of particles lead to increment of specific surface area and cause improve in solubility.[29] In vitro dissolution rate was determined for pure Ibuprofen and the best formula(F4), the result show that at time 15 min 98% of drug release of formula F4 while only 25% of pure Ibuprofen, however, Ibuprofen nanoparticles show increment in dissolution rate relate to pure drug. These results as decrease in the size of particles lead to enhance the surface area and improve in dissolution rate as well as improve in bioavailability.[30,31]

CONCLUSION

Ibuprofen nanosuspensions were prepared by using solvent antisolvent precipitation method by using different type of polymers (pvpk30, poloxamer188 and HPMC E50) with different concentration (1:1, 1:2 and 1:3). The research demonstrates that Ibuprofen nano suspension (123nm) with pvpk30 at ratio 1:1 drug: stabilizer successfully works. Spherical shape of particles without the sign of aggregation of nanoparticles was detected by SEM. The dissolution rate show enhancement with improve in saturated solubility due to decrease in the size of particle with increase in surface area.

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CONFLICT OF INTEREST
Authors declare no conflict of interest.
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AUTHORS' CONTRIBUTION

The following authors have made substantial contributions to the manuscript as under:

Conception or Design:	FMHW, AWA
Acquisition, Analysis or Interpretation of Data:	FMHW, AWA, MHO
Manuscript Writing & Approval:	FMHW, AWA, MHO

All the authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.