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Research Article

Formulation and Characterization of Oral Suspension Containing Ibuprofen

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ABSTRACT

The present work was aimed with the objective of formulating oral suspension of ibuprofen to enhance the convenience and compliance by the elderly and pediatric patients. The suspension were prepared by incorporating the prepared ibuprofen physical mixtures so as to achieve the aimed percent drug release (using poloxomer, Poly vinyl pyrrolidone (PVP and PolyVinaylAlcohol (PVA)) in sodium carboxy methyl cellulose as dispersing medium. Particular attention was given to the selection of the suitable taste masking agents. The suspension was characterized in term of ibuprofen content, viscosity, and sedimentation volume and dissolution test. The promising suspension F8 having the optimal formula showing the greatest dissolution and satisfactory sedimentation volume and physico-mechanical properties compared with a reference marketed product. FT-IR studies revealed that there is no interaction between the drug and the polymers used in the study. Rheological studies revealed significant difference between the suspensions that the incorporation of PVP and PVA enhances the viscosity of the suspension as a result the rate of dissolution was retarded.

Key-words: Ibuprofen, suspension, PVA, PVP, Poloxomer

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INTRODUCTION

Analgesic medications are a first line of treatment in acute pain cases, and all practitioners should be familiar with their use. Aspirin, Acetaminophen, and Nonsteroidal Anti-Inflammatory Agents (NSAIDS) like Ibuprofen (IBU). All these compounds inhibit cyclooxygenase (COX), and, except for acetaminophen, all have anti-inflammatory actions, especially at higher dosages. They are particularly effective for mild to moderate headache and for pain of musculoskeletal origin.

Pharmaceutical suspensions are uniform dispersions of solid drug particles in a vehicle in which the drug has minimum solubility. A suspension containing particles between 1 nm to 0.5 μ m in size is called colloidal suspension. When the particle size is between 1 to 100 μ m, the suspension is called coarse suspension. Most of the pharmaceutical suspensions are coarse suspension. Majority of the available suspensions in the market are ready-to-use but occasionally some products are available as dry powders which must be reconstituted before administration. Particle size of the drugs may vary from one formulation to the other depending on the physicochemical characteristics of the drug and the rheological properties of the formulation.

Factors to be considered during the formulation of the suspension are sedimentation rate, particle size and viscosity of the vehicle. Ibuprofen chemical name is 2-[4-(2-methylpropyl) phenyl] propanoic acid. It is used for the treatment of analgesic, antipyretic, and anti-inflammatory activity. The present investigation was aimed at developing oral administrable pharmaceutical formulations of IBU with improved dissolution properties. Ibuprofen chemical name is 2-[4-(2-methylpropyl)phenyl]propanoic acid. It is used for the treatment of analgesic, antipyretic, and anti-inflammatory activity.Suspensions are prepared majorly by mortar and pestle in lab scale method where as for large scale preparations homogenizer is used.

The present investigation was aimed at developing oral administrable pharmaceutical formulations of IBU with improved dissolution properties.

METERIALS AND METHODOLOGY

MATERIALS

Ibuprofen was gift sample obtained from Divispharmapvt ltd, Hyderabad. PVA, PVP and poloxomer was purchased from Loba Chemicals. Sucrose and sodium Meta bisulphate was obtained from Qualigenspharma. Glycerol was secure from Merck pharma ltd.

METHODOLOGY

Preformulation studies

Organoleptic Properties:

The drug sample was viewed visually and viewed under the compound microscope for the determination of its color using the black and white backgrounds and nature of the drug sample. Then the results were compared with the official books and United States Pharmacopoeia.

Solubility:

The solubility of the drug sample was carried out in different solvents (aqueous and organic) according to the Indian Pharmacopoeia. The results are then compared with those given in the official books.

FT-IR studies:

Compatibility between the drug and excipients was important during the formulation. These studies were carried out using FTIR studies. Drug and excipients were prepared in differ ratios for the analysis. The freshly prepared drug and excipient mixtures spectra were recorded by using FT-IR. Then the mixtures were examined for their compatibility was analysed by comparing the recorded spectra.

Construction of calibration curve:

Calibration curve of ibuprofen was constructed by using a series of standard solutions containing 11, 12, 13, 14, and 15 μg of ibuprofen per ml. The solutions were scanned in the region 200 - 400 nm using ELICO-SL 159 UV

spectrophotometer and the absorbance of the solutions were measured at 221 nm using pH 7.2 phosphate buffers as a blank. The calibration curve of ibuprofen was shown in Figure 1.

Preparation of Suspension:

- The suspensions were prepared by mortar and pestle.
- 125 mg of ibuprofen was taken in a mortar to it Poloxomer/ Poly vinyl pyrrolidone / Poly vinyl alcohol was added to the mortar in geometric dilution with intermittent mixing along with the glycerol and syrup.
- The product was collected and triturated thoroughly for uniform mixing. 5 ml of suspension in which 125 mg equivalent of ibuprofen was accurately weighed and stored until further use.

Table 1: Composition of Ibuprofen Oral Suspension

S.No	Ingredients (mg)	A	B	C	D	E
1	Ibuprofen	125	125	125	125	--
2	PVP	--	125	--	--	--
3	PVA	--	--	125	--	--
4	Poloxomer	--	--	--	125	--
5	Marketed product	--	--	--	--	125

Evaluation of suspension

Drug content:

5ml of suspension equivalent to 125mg of ibuprofen was taken in a 100ml volumetric flask, 10ml ethanol and 20 ml of pH 7.2 Phosphate buffer was added and the contents were sonicated for 10min and made up to the mark with pH 7.2 phosphate buffer. This solution was suitably diluted with pH 7.2 phosphate buffer and was assayed at 221nm for Paracetamol.

Rheological Studies:

The viscosity was measured using Brookfield DV-II + PRO viscometer. The formulation was taken into the cup of viscometer and measured using spindle CP64 at the rotation of 60 rpm. The viscosity measurements were measured in triplicate using fresh samples each time.

Stability Studies:

The stability studies were carried out by ageing method storing the formulations at ambient temperature in measuring cylinder. The suspensions were analyzed at end of 24hrs to calculate the sedimentation volume.

$$F = Vu / Vo$$

Where

F = Sedimentation volume

Vu = Final volume of sediment

Vo = Original volume of suspension before settling

Dissolution rate studies:

The dissolution rate testing of ibuprofen suspension was studied using USP XXII dissolution rate testing apparatus, (paddle type) (LAB INDIA DISSO 2000). The paddle was rotated at a speed of 50 rpm and the dissolution fluid (900 ml pH 7.2 Phosphate buffer) was maintained at a temperature of $37.5^0 \pm 0.5\ ^0C$. At specific time intervals a 5 ml aliquot of dissolved medium was withdrawn and was replaced with fresh quantity of dissolution medium. The samples were suitably diluted with dissolution medium and assayed for ibuprofen content by measuring the absorbance at 221 nm using U.V Spectrophotometer (ELICO SL 159). The percent of ibuprofen dissolved at various time intervals was calculated and plotted against time. The results are given in table. Graphical plots of % dissolved versus time and ln(% undissolved) versus time, % drug

dissolved versus Alldissolution studies were carried in triplicate. From the dissolution profiles of all prepared formulations the best one is evaluated.

RESULTS &DISCUSSIONS

FT-IR STUDIES:

The FT-IR spectra of the drug and excipients were given as figures (2-). It was concluded that there is no compatibility between the drug and the excipients as no new peaks were produced. However there was only reduction in intensity of peaks due to dilution of the drug with excipients.The FTIR spectra for the mixtures were shown in figures 2-6.

EVALUATION OF SUSPENSIONS

Assay of the drug content:

All the oral suspensions prepared by the using mortar and pestle were found to contain 95% to 105% of the amount that should contain.

The assay results of various formulations are given in the Table 2.

Rheological behavior of ibuprofen suspensions:

Viscosity is one of the important parameters which provide vital information during the optimization of the suspension formulation. In general, the viscosities of the prepared suspensions are in the range of 50-400 reported in the Table 2.

From the above results we can observe that the viscosity of the first five formulations (F1 – F5) are more when compared to the remaining formulations. Moreover the viscosity has linearly increased from F1 to F5. This indicates that as the concentration of PVP in the formulation affecting the viscosity of the respective formulation. May be due to the binding property of the PVP as binder concentration increases the consistency and the sticky nature of the suspension has increased which leads to the increase in the viscosity of the suspension. The formulations from F6 to F9 have shown an average of 40 cps of viscosity which were formulated using PVA which is also a binder, but showing less extent of binding capacity (swelling) compared to PVP Again the final formula showed increase in the viscosity due to the addition of PVP.

Dissolution Rate Studies

The percent of ibuprofen dissolved at the various time intervals were calculated and plotted against time. The results were given in the Table 3-4, graphical plots of percentage of ibuprofen dissolved versus time, Log of percentage of ibuprofen un dissolved versus time are given in figure 7-8 and also calculated the half life(t_{50}),first order rate constant(k_1),percentage of dissolution efficiency (%DE). The dissolution data reveals that the formulation F8 shows better release than the other formulations containing PVP and PVA.

Stability studies:

The overall stability of a suspension depends on its sedimentation rate. So, the suspension having low sedimentation volume has the better stability. In general the sedimentation volume of suspension formulations are equal to 1 (F=1). The sedimentation volume of formulations is given in Table 2.

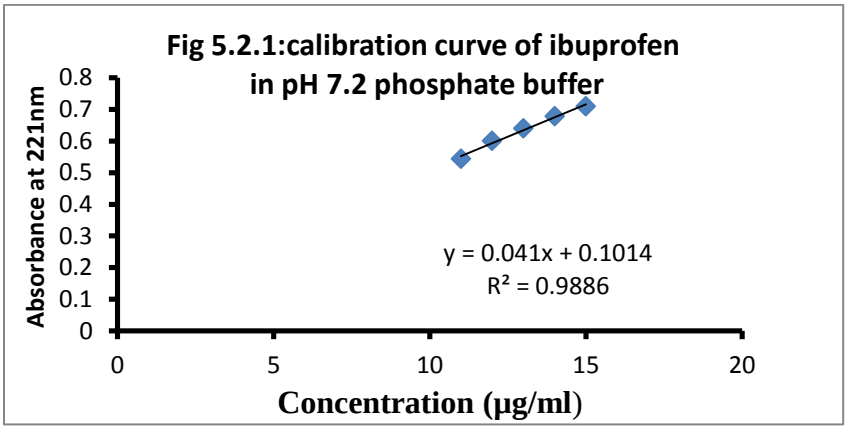

Figure 1: Calibration curve of Ibuprofen in pH7.2 phosphate buffer

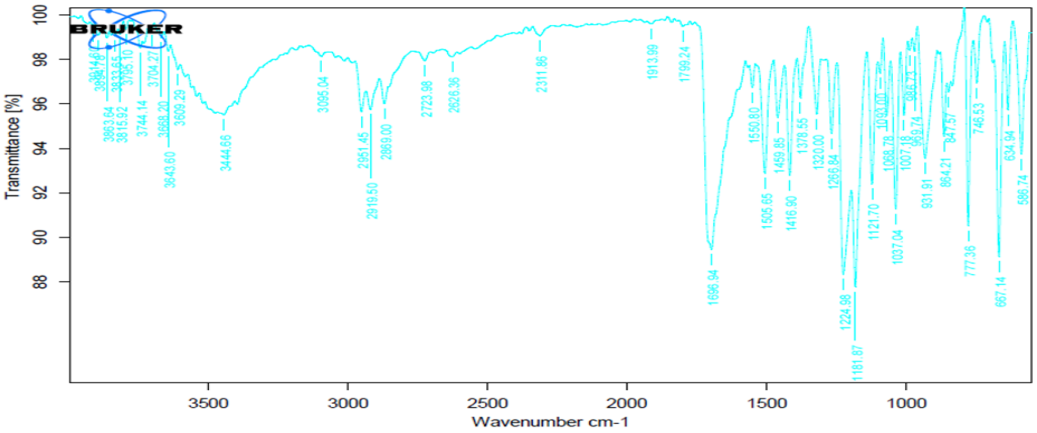

Figure 2: FT-IR Spectra of Pure Ibuprofen

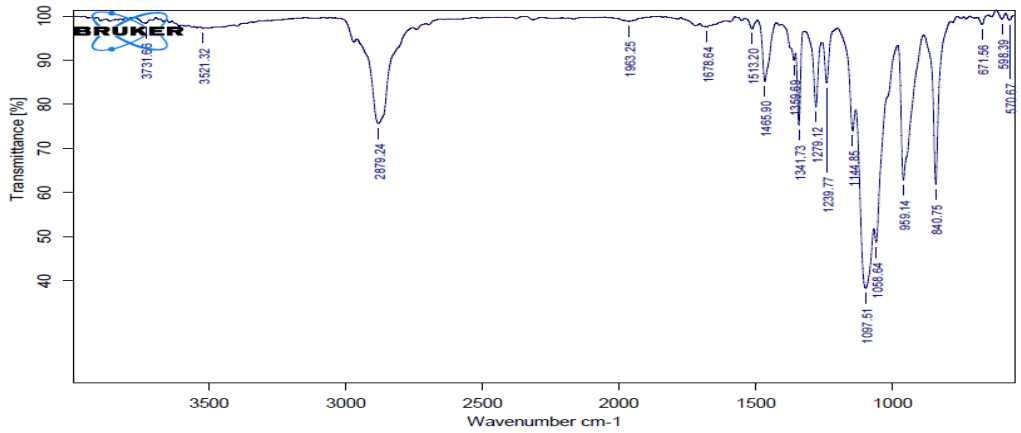

Figure 3: FT-IR Spectra of Poloxomer

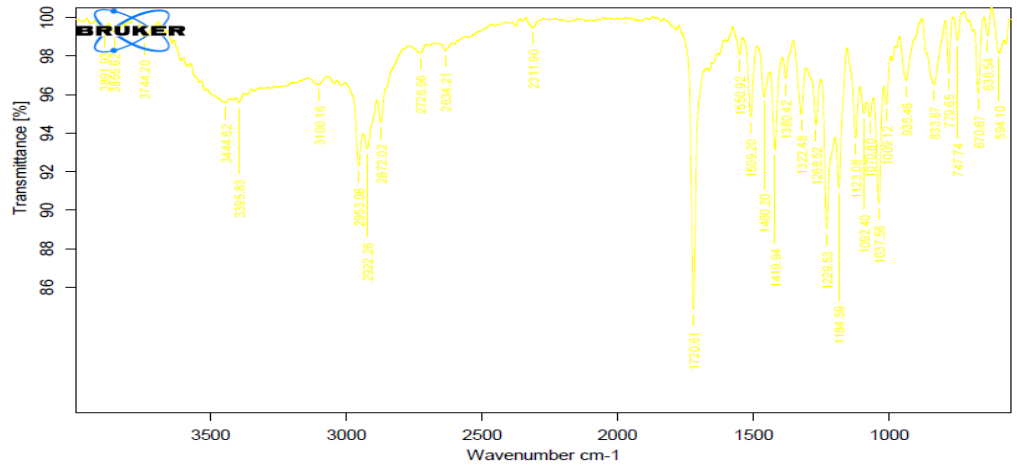

Figure 4: FT-IR Spectra of PVA

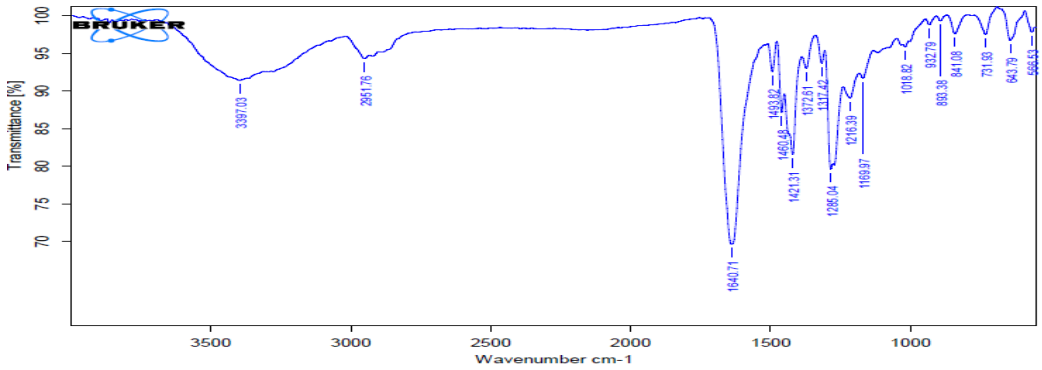

Figure 5: FT-IR Spectra of PVP

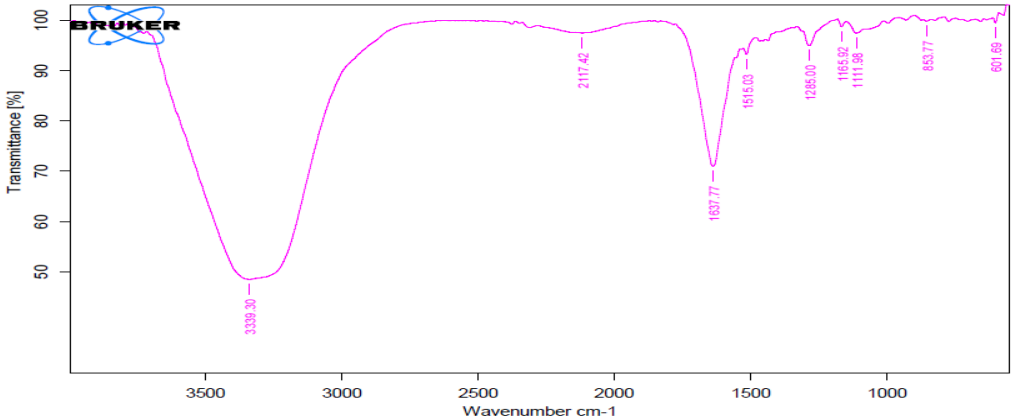

Figure 6: FT-IR Spectra of final formulation

Table 1: Formula used for preparation of suspension

Formulation code	F1	F2	F3	F4	F5	F6	F7	F8	F9	F10
Ibuprofen	200	200	200	200	200	200	200	200	200	200
Polyvinyl	-	-	5	5	5	-	-	-	-	-

pirrolidone(mg)										
Polyvinyl alcohol(mg)	-	-	-	2.5	5	-	-	-	-	2.5
Sodium CMC(Q.S)	Q.S	-	Q.S	Q.S	Q.S	Q.S	Q.S	Q.S	Q.S	Q.S
Methyl paraben(mg)	2	-	2	2	2	2	2	2	2	2
Sodium citrate(mg)	0.02	-	0.02	0.02	0.02	0.02	0.02	0.02	0.02	0.02
Poloxomer(mg)	-	-	-	-	-	25	50	75	100	100
Orange essence(ml)	0.1	-	0.1	0.1	0.1	0.1	0.1	0.1	0.1	0.1
Sodium meta bisulphate(mg)	0.01	-	0.01	0.01	0.01	0.01	0.01	0.01	0.01	0.01
Glycerol(ml)	-	-	2	2	2	2	2	2	2	2
Vanillin(mg)	5	-	5	5	5	5	5	5	5	5
Tween 80(ml)	0.1	-	0.1	0.1	0.1	-	-	0.2	0.5	0.5
Syrup(ml)	5	-	5	5	5	5	5	5	5	5
Sunset yellow(ml)	0.1	-.	0.1	0.1	0.1	0.1	0.1	0.1	0.1	0.1
Total volume(ml)	10	-	10	10	10	10	10	10	10	10

Table 2: Evaluation parameters of suspension

S.No.	Formulation	Viscosity(cps)	%Assay	Sedimentation volume
1	F1	359	100	1
2	F2	444	99.7	0.99
3	F3	599	98.9	0.99
4	F4	479	102	1
5	F5	549	98.6	1
6	F6	40	97.4	0.94
7	F7	43	105.7	0.96
8	F8	40	103.6	0.99
9	F9	40	101.4	0.96
10	F10	50	104.8	1

Table 3: Comparative Dissolution profile of ibuprofen suspension

S.No	Time (min)	% Drug Dissolved									
		F1	F2	F3	F4	F5	F6	F7	F8	F9	F10
1	0	0	0	0	0	0	0	0	0	0	0
2	5	13.79	53.57	45.77	43.12	35.21	68.71	75.51	91.12	84.81	81.09
3	10	22.501	54.36	47.18	44.56	37.44	73.98	80.1	93.89	89.59	85.16
4	20	28.74	56.24	49.1	46.43	39.93	78.8	85.49	96.3	94.14	88.34
5	30	37.19	58.06	51.23	48.4	42.12	84.22	89.67	97.86	98.18	91.55
6	45	50.144	61.25	57.02	50.1	45.12	91.18	95.88	99.16	100.71	98.03
7	60	60.166	63.25	59.37	51.75	47.33	97.13	100	101.27	104.78	102.46

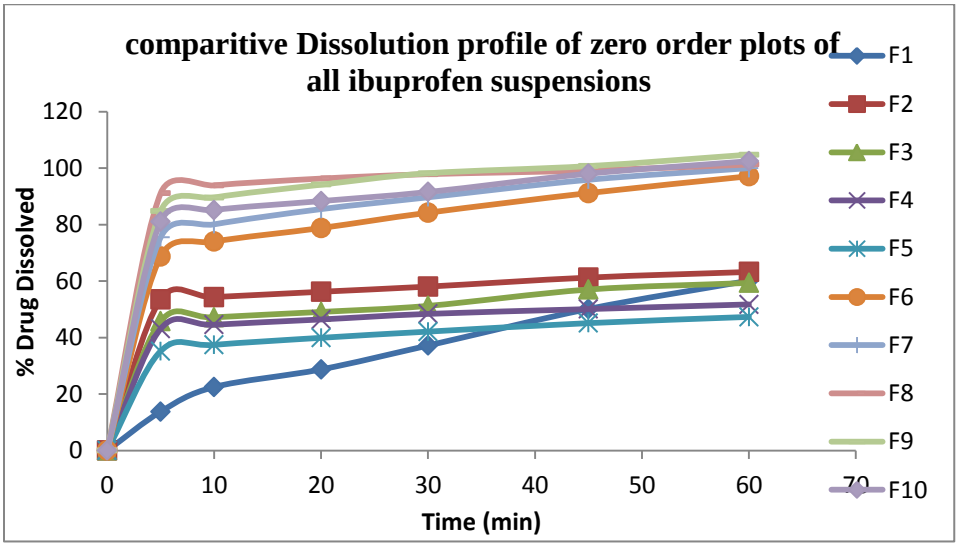

Figure 7: comparative dissolution profile of zero order plots all formulations (F1-F10)

Table 4: Comparative profile of log % drug undissolved of all ibuprofen formulations

S.No	Time (min)	F1	F2	F3	F4	F5	F6	F7	F8	F9	F10
1	0	0	0	0	0	0	0	0	0	0	0
2	5	13.79	53.57	45.77	43.12	35.21	68.71	75.51	91.12	84.81	81.09
3	10	22.501	54.36	47.18	44.56	37.44	73.98	80.1	93.89	89.59	85.16
4	20	28.74	56.24	49.1	46.43	39.93	78.8	85.49	96.3	94.14	88.34
5	30	37.19	58.06	51.23	48.4	42.12	84.22	89.67	97.86	98.18	91.55
6	45	50.144	61.25	57.02	50.1	45.12	91.18	95.88	99.16	100.71	98.03
7	60	60.166	63.25	59.37	51.75	47.33	97.13	100	101.27	104.78	102.46

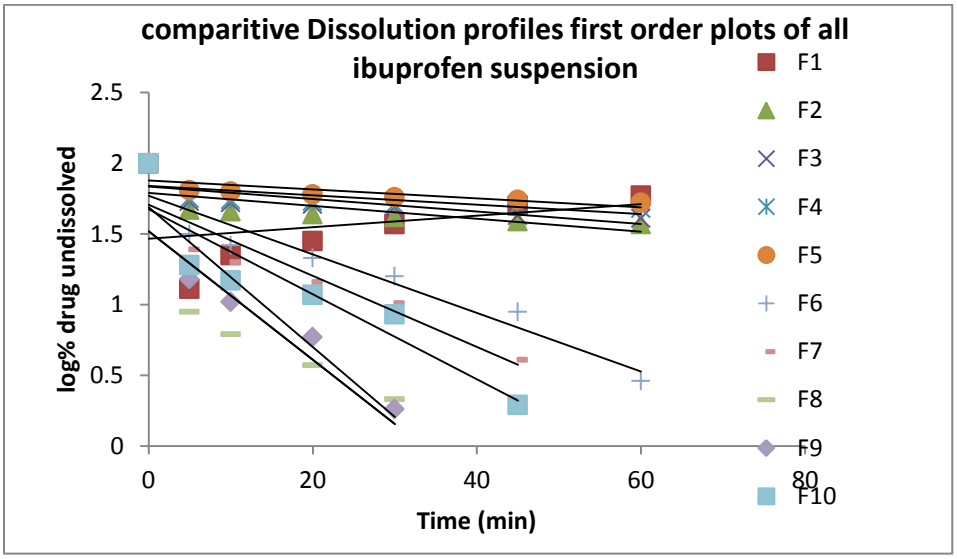

Figure 8: comparative dissolution profile first order plots of all formulation (F1-F10)

CONCLUSION

Suspensions of Ibuprofen were prepared using PVP, PVA, was found to perform better than the pure drug with respect to the dissolution. Formulation with poloxomer and syrup as dispersing medium has shown maximum drug release and apart to mask the taste than the marketed tablet. The dissolution data reveal that here is no significant difference between the suspension F8 and F10 (marketed product). However *in-vivo* studies are needed to prove that.

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