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DESIGN AND OPTIMIZATION OF FAST DISSOLVING IBUPROFEN TABLET INCORPORATING DIFFERENT POLYMER AND SUPERDISINTEGRANTS

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ABSTRACT

Poor water solubility is characterized by low dissolution rate and consequently reduced bioavailability. Formulation of solid dispersion has attracted considerable interest where dispersing a poorly water soluble drug in a water soluble polymer matrix improves the dissolution characteristics and bioavailability of the drug.Solid dispersions of Ibuprofen with mannitol, polyethylene glycol 4000, and polyvinyl pyrrolidone K-32, were prepared with a view to increase its water solubility. Ibuprofen solid dispersion was prepared by solvent evaporation method. Effects of different polymer i.e. mannitol, polyvinylpyrrolidone (PVP) K32 and PEG 4000 were studied for solid dispersion. Solid dispersions were investigated for drug content and dissolution characteristics.Solid dispersion of Ibuprofen containing PVP-K32 at the ratio of drug: polymer 1:4 showed faster and higher drug release. Further it was found that fast dissolving tablets containing pregelatinized starch as superdisintegrant showed maximum % drug release (90 %) in first 20 sec as compared to formulation containing sodium starch glycolate.

INTRODUCTION

A poorly water-soluble drug often shows insufficient bioavailability due to its poor solubility and low dissolution rate, especially for Biopharmaceutics Classification System (BCS) class II drugs. This series of drugs possess low solubility but high permeation and the bioavailability can be greatly improved by accelerating the dissolution process in the gastrointestinal tract. For increasing the dissolution rate by enhancing its specific surface area or solubility has taken into consideration, such as micronization, enhancing the wettability and solid dispersion technology [1]. Therefore, poorly aqueous soluble drugs characterized by low bioavailability is a major concern of pharmaceutical industries worldwide [2]. With the recent advent of high throughput screening of potential therapeutic agents, the number of poorly soluble drug candidates has risen sharply and the formulation for oral delivery presents one of the most frequent and greatest challenges to formulation scientists [3].Among various approaches, the solid dispersion technique has been widely and successfully applied to improve the solubility, dissolution rates and consequently bioavailability of poorly water soluble drugs[4]. Though ibuprofen is absorbed rapidly and bound to protein, it is not showing complete therapeutic effect because of their poor solubility and disso lution, which leads to poor bioavailability of the drug[5,6].

Now a days, importance is given to enhance the dissolution rate of the poorly soluble drugs, so, it increases the bioavailability of drug, so that solid dispersion is one of the techniques used to increase the dissolution rate of the lipophilic drugs[7-9]. Solid dispersions are prepared by solvent or co-precipitation method where both guest solute and solid carrier solvent are dissolved in a common volatile solvent such as alcohol. The liquid solvent is removed by evaporation under reduced pressure or by freeze drying which results in amorphous precipitation of guest in a crystalline carrier [10,11].

Present investigation explores the enhancement of solubility and dissolution of Ibuprofen. Ibuprofen was chosen as model drug because it is a phenyl propionic acid derivative, widely used as first line non-steroidal anti-inflammatory (NSAID), analgesicand antipyretic agents with a half-life of 1.8-2 h[12]. It is also used to relieve headaches, muscle aches, tenderness, menstrual pain, aches and pains from the common cold, backache and pain in post-surgery or dental pain and stiffness caused by arthritis and gout. Ibuprofen is a core medicine in the World Health Organization's "Essential Drugs List", that means it is in list of minimum medical needs for a basic health care system [13]. It is a poorly aqueous soluble drug and its oral absorption is

dissolution rate limited, which leads to a potential bioineqivalence problem. Thus, the improvement of Ibuprofen dissolution for its immediate release is desirable for rapid Ibuprofen absorption, which is prerequisite for quick onset of its pharmacological actions.

MATERIALS AND METHODS

Ibuprofen pure drug was obtained as gift sample of SunPharmaceuticals, Ahmadabad. Mannitol, polyvinylpyrrolidone (PVP K-30) were purchased from Central Drug House, New Delhi. Poly ethylene glycol (PEG 4000) was purchased from G. S Chemical Testing Lab and Allied Industries,Mumbai. Acetone was purchased from Qualigens Fine Chemicals, Mumbai.

Preparation of solid dispersion

Solid dispersion was prepared using solvent evaporation method. Accurately weighed amount of Ibuprofen and carriers likepolyethylene glycol 4000 (PEG 4000), polyvinyl pyrrolidone K-30 (PVP-K30) and mannitol were taken in 1:1, 1:2 and 1:4 ratio each forms formulation F1 to F9 (Table1) in glass beaker and dissolved in ethanol to obtain a clear solution. This solution was stirred robustly for uniform mixing and evaporated at room temperature. The viscous residue obtained was passed through sieve and solid dispersion was obtained.

Table 1:Composition of solid dispersion

Sl. No	Ingredients	Pure drug	Formulation code of solid dispersion								
			F1	F2	F3	F4	F5	F6	F7	F8	F9
1	Ibuprofen	50 mg	50 mg	50 mg	50 mg	50 mg	50 mg	50 mg	50 mg	50 mg	50 mg
2	Mannitol	-	1:1	1:2	1:4	-	-	-	-	-	-
3	PEG 4000	-	-	-	-	1:1	1:2	1:4	-	-	-
4	PVP- K32	-	-	-	-	-	-	-	1:1	1:2	1:4

In vitro dissolution study of solid dispersion

The release profile of solid dispersion of formulationsF1 to F9 were assessed using *in vitro* dissolution apparatus (USP XXI, six stage) using phosphate buffer pH7.2 at 50 rpm. Samples were collected at regular time interval of 10 min and were analyzed in UV spectrophotometer (Shimadzu 1600) at wavelength 221nm. Drug release obtained was given in Table 2.

Table 2: Percentage releases of solid dispersions with different carriers

Times (mins)	Pure drug	Mannitol			PEG 4000			PVP- K32		
		F1 (1:1)	F2 (1:2)	F3 (1:4)	F4 (1:1)	F5 (1:2)	F6 (1:4)	F7 (1:1)	F8 (1:2)	F9 (1:4)
0	0	0	0	0	0	0	0	0	0	0
10	27.15	45.12	29.37	37.5	32.45	28.17	40.67	29.24	47.22	50.0
20	33.11	50.72	48.67	42.5	35.07	35.97	61.55	42.98	47.92	-67.5
30	37.20	53.72	57.27	45.0	42.15	46.72	69.77	56.58	52.62	72.5
45	45.01	58.20	69.55	50.0	52.97	62.30	77.97	62.56	53.67	75.0
60	53.94	65.65	76.82	57.5	54.47	73.05	78.72	71.53	61.55	87.5

Preparation of fast release tablet using solid dispersion

Among various formulations, F6 and F9 were selected as optimized formulations due to higher drug release rates. Drug: polymer (1:4) of PEG 4000 and PVP-K30 respectively were used for preparation of fast release tablet by direct compression method using two different superdisintegrantspregelatinized starch and sodium starch glycolate forming formulation B1, B2, B3 and B4 shown in Table 3.

Table 3: Composition of fast release ibuprofen tablet containing optimized solid dispersion

Sl.No	Ingredients	B1(mg) F6 with PS	B2(mg) F9 with PS	B3(mg) F6 with SSG	B4(mg) F9 with SSG
1	Solid dispersion (equivalent to 20 mg drug)	70.92	54.05	70.92	54.05
2	Sodium starch glycolate (SSG)	-	-	9	9
3	Pregelatinized starch (PS)	9	9	-	-
4	Magnesium stearate	1.8	1.8	1.8	1.8
5	Talc	3.6	3.6	3.6	3.6
6	Microcrystalline cellulose	47.33	47.33	47.33	47.33
7	Lactose	47.33	55.7	47.33	55.7

***In vitro* dissolution study of fast release tablet**

In vitro dissolution study was performed ondissolution apparatus (USP XXI, six stage) and samples were collected at regular interval of 10 min. The samples were further analyzed spectrophotometrically.

RESULT AND DISCUSSIONS

Solid dispersions prepared using mannitol, PEG 4000 and PVPK32 in drug: polymer ratio of 1:1, 1:2 and 1:4 each. Graph plotted between % drug release andtime for all the three carriers were shown in Fig1, 2 and 3 respectively;which exhibits that as the concentration of polymerincreases, the percentage of drug release also increases.There was increase in solubility because of increase in wettability by the carriers which causes increased percentage of drug release. From the data obtained from Table 4 and also Fig 4 shows that F9 formulation (containing PVPK30) has maximum dissolution rate[14] than PEG and pure drug (drug: polymer, 1:4). The reason for the poor dissolution of pure drug could be of poor wettability and, or agglomeration of particles.

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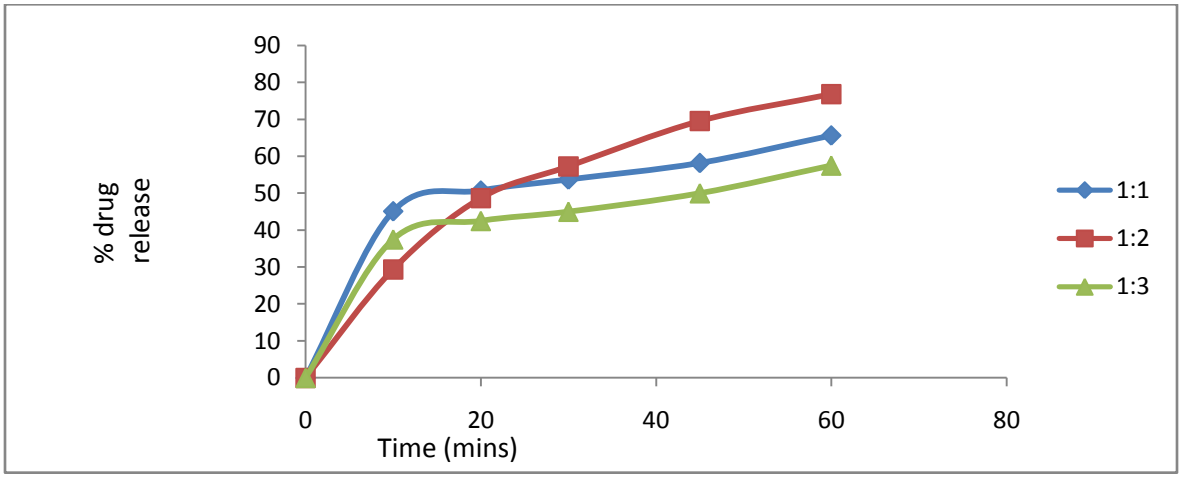

Fig1:Comparative % drug release of solid dispersion of drug:mannitol in different ratios

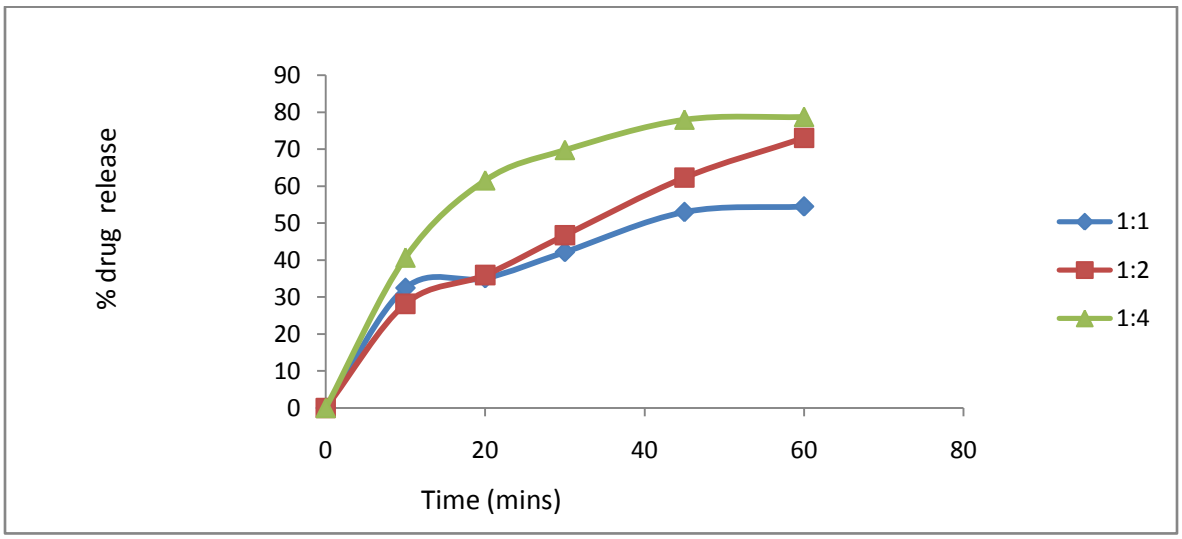

Fig 2:Comparative % drug release of solid dispersion of drug: PEG 4000 in different ratios

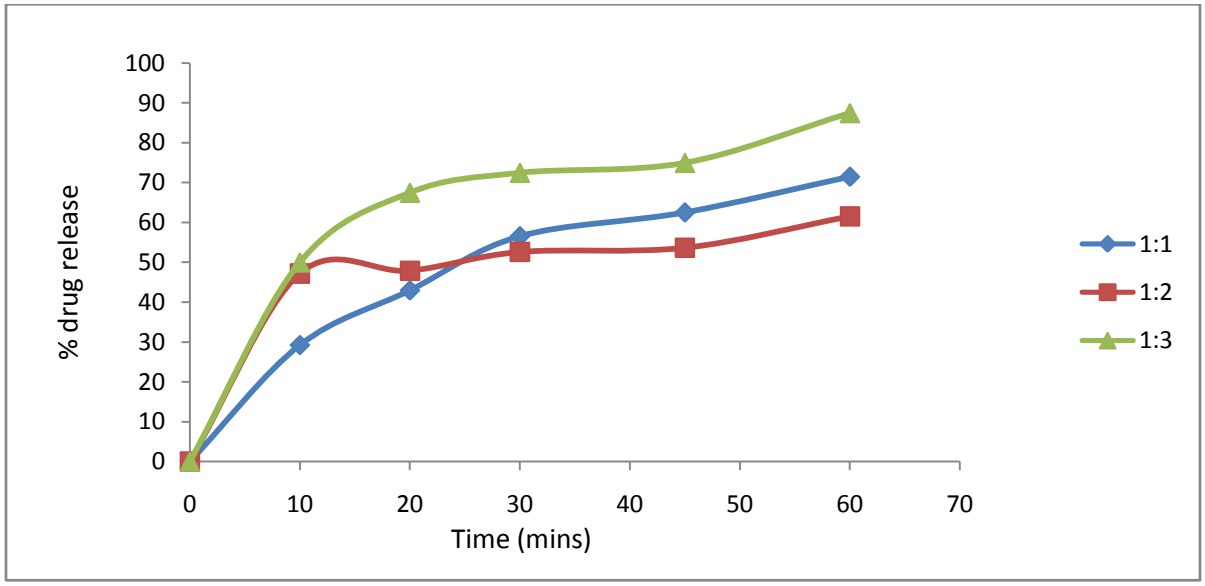

Fig3:Comparative % drug release of solid dispersion of drug: PVPK-32 in different ratios

From Fig. 1, 2 and 3;formulations F3, F6 and F9 of solid dispersions having maximum percentage of drug release. So the optimized dispersions were F6 and F9 with drug: PEG 4000 (1:4)and drug: PVPK30 (1:4) respectively. The reason for lesser release rate with PEG4000 (drug: polymer, 1:4) in comparison to PVPK30 (drug: polymer, 1:4) solid dispersion may be due to the presence of crystallinity in PEG dispersion and improper wetting of drug with PEG which results lower release rate in comparison to PVP dispersion.

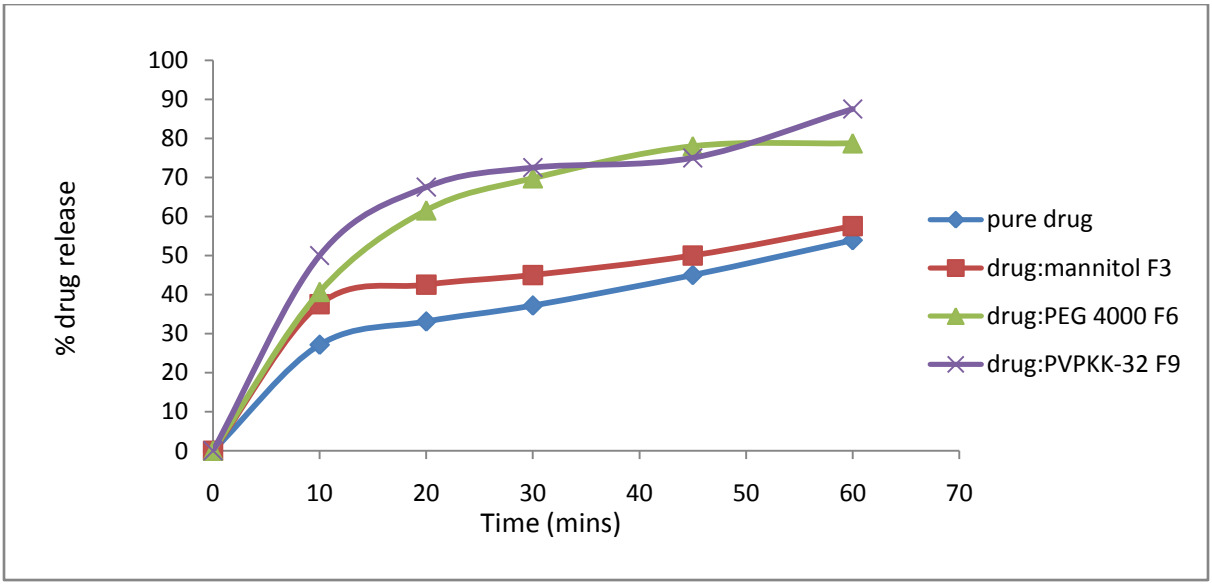

Fig 4:Comparative % drug release of solid dispersionsusing different carriers giving best result

After preparing fast dissolving tablets of Ibuprofen containing solid dispersion of Ibuprofen-PVPK30 and Ibuprofen- PEG 4000 in 1:4 ratio by using two superdisintegrant, the results obtained is shown in Table 4.

Table4: Evaluation parameters of prepared fast release tablets

Sl. No	Parameter	Formulation code of tablets			
		B1	B2	B3	B4
1	Hardness (kg/cm)	4.4	3.0	2.5	5
2	% drug release (at 20 mins)	54.68	90.33	58.06	31.25
3	Dissolution efficiency (%)	31.5	59.25	42	18.25
4	Drug content	20.09	43.23	21.27	24.0

Table 5:Percentage release of fast release tablet using two superdisintegrants

Time (mins)	B1 (F6 with PS)	B2 (F9 with PS)	B3 (F6 with SSG)	B4 (F9 with SSG)
0	0	0	0	0
10	35.71	75.52	55.27	20.80
20	54.68	**90.33**	58.06	31.25
30	68.08	85.85	62.96	35.42
45	77.01	68.15	65.96	54.46
60	82.29	59.19	70.65	70.80

After that, optimized formulation F6 and F9 solid dispersions were selected, as they showed maximum % release, for formulationof fast release tablet with two different superdisintegrants codedas B1, B2, B3 and B4. From Table 5, graphs between % drug release and time was plotted (Fig4) which shows that B2 shows highest percentage of drug release 90.33% in 20sec as compared to other whichconcludes to result that tablet with pregelatinized starch as superdisintegrant is better than tablet with sodium starch glycolate[15]. So the best tablet obtained containing PVPK32 polymer with pregelatinized starch as superdisintegrant.

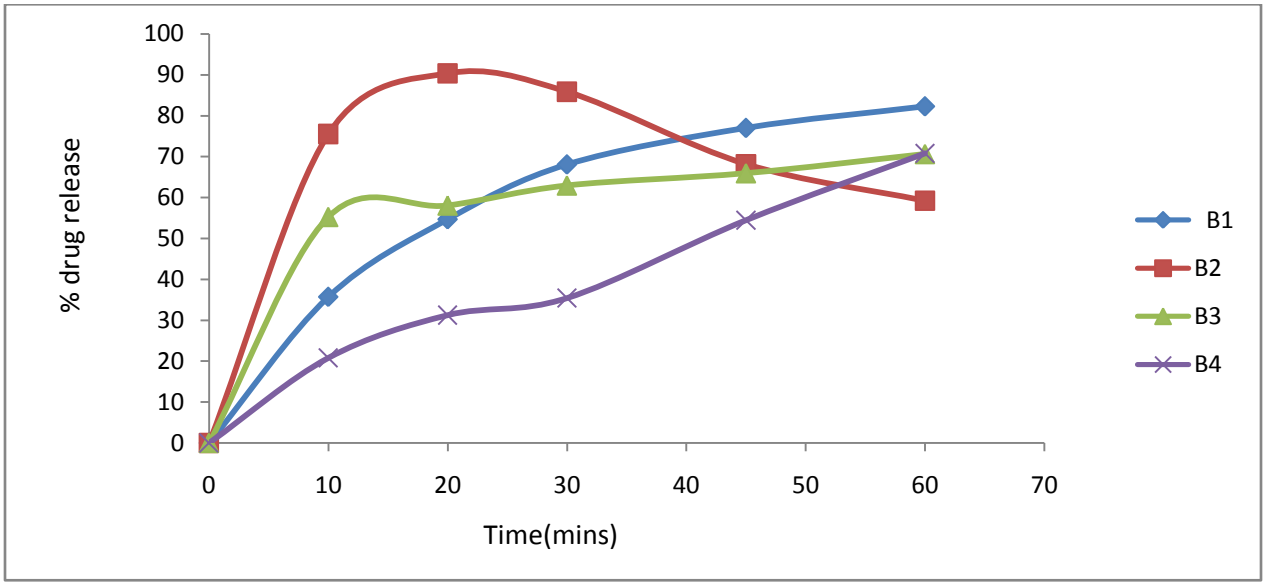

Fig 5:Comparative % drug release of fast dissolving tablet using different superdisintegrants

CONCLUSION

The present investigation successfully formulated fast dissolving tablets of oxcarbazepine with improved drug release profile. Solid dispersion technology was employed for the formulation of fast dissolving tablets. It has been concluded that solid dispersion having PVPK32 is better polymer than PEG 4000 and also pregelatinized starch is better superdisintegrant than sodium starch glycolate in fast dissolving ibuprofen tablet containing solid dispersion.

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