Bull. Pharm. Sci., Assiut University
Vol. 7 part 2, pp. 295 - 304

ENHANCED DISSOLUTION RATE OF IBUPROFEN USING SURFACTANTS AND WATER SOLUBLE CARRIERS

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ABSTRACT

The influence of some non-ionic surfactants as well as polyethylene glycol 6000 and dextrose as water soluble carrier, on the dissolution of poorly soluble drug, ibuprofen, was studied. Surfactants produced better drug release than the polyethylene glycol and dextrose with the drug carrier ratio studied. TLC and IR studied ruled out any interaction between the drug and any of the additives used. In addition, the bulkness of the drug was not affected by the amount of surfactants added, as being found with dextrose and polyethylene glycol 6000.

INTRODUCTION

For several years, it has been recognised that the availability of a drug for gastrointestinal absorption from solid dosage form is even relfected by the in-vitro dissolution rate. Many investigations have been carried out on enhancement the solubility and dissolution rate of slightly soluble drugs by the utilization of coprecipitates using water soluble carriers [1-9].

Differential thermal analysis[10], IR spectral analysis[11], X-ray diffraction[12], microscopic examination[10] and TLC[11,13] were some of the intensive study reported to explain the mechanism underlying the influence of polyethylene glycol in

enhancing the dissolution rate of drugs. Each of these approaches for increasing the dissolution rate requires a unique type of drug molecule[14]. Crystallization of sulfathiazole , prednisone and chloramphenicol in aqueous surfactants solution exhibited increased dissolution rates[15].

The purpose of this investigation is to report two different methods to enhance dissolution rate of poorly water soluble drug namly, Ibuprofen, coprecipitated with suractants and water soluble compounds as carriers.

EXPERIMENTAL

Materials:

Ibuprofen (Boots Pure Drug Co. Ltd. Nottingham,England), Polyethylene glycol 6000 (B.D.H. England), Tween 20,80 and Myrj 53 (Atlas Chem. Indust. USA), Dextrose anhydrous(El-Nasr Chemical Co. Egypt.) All Chemicals used were fine grades.

Methods:

Preparation of Ibuprofen Coprecipitates.

A- Using water-soluble carriers

By mixing ethanolic solutions of the drug and P.E.G. 6000, the copecipitates were prepared in different drug-carrier ratio ranging from(2:1), (1:1) and (1:2). The solvent was evaporated on water bath until complete dryness. The same method was repeated using anhydrous dextrose instead of PEG 6000.

B- Using non-ionic surfactants

The same technique as mentioned before was applied using surfactants concentrations ranging from 2.5 to 10% w/w.

C- Treatments of the prepared coprecipitates

The resulted coprecipitates were placed in a disiccator for 24 hours. All preparations were reduced to particle size of 100-200 μ and kept in disiccator for in-vitro dissolution studies. Ibuprofen was treated alone using the same method and under the same conditions. The The same particle size range served as control.

Dissolution rate studies

The dissolution apparatus was exactly similar to that employed by Levy and Hayes[16]. The dissolution study was carried out on these preparations in 500 ml of distilled water. The dissolution medium was maintained at 37 + 0.5° and stirred at 100 rpm. The test preparations were filled into capsules, each containing a quantity equivalent to 100 mg drug. At certain time intervals, 2.0 ml aliquot was withdrawn, filtered and replaced with the same amount of the fresh dissolution medium. The concentration of the drug in solution was determined spectrophotometrically[1] at 222 nm.

IR Spectral analysis

The IR spectra of the drug alone and in form of coprecipitates were recorded using potassium bromide pellets[2].

U.V. Spectroscopic analysis.

The U.V. spectroscopic analysis of the drug and its copricipitates was determined in the range between 200 and 300 nm.

Thin-layer Chromatography (TLC)

A slurry of silica gel G was spread on plates of 0.25 mm thickness. The solvent system was benzene ether-glacial acetic

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[1] Pye Unicam Sp 16000

[2] Pye Unicam 1000.

acid-methyl alcohol (120:60:18:1). 10 ml aliquots of 0.1% alcoholic solution of the drug and its preparations were spotted on the plates and developed. The visualization of the spots was made by spraying with 1% solution of Potassium permanganate[17].

RESULTS AND DISCUSSION

The results of the dissolution studies, expressed in the amount (mg) of drug released per 100 ml. as a function of time, for ibuprofen alone and coprecipitated with both, non-ionic surfactants and water soluble carriers, are shown in Figure 1. All preparations yielded faster Ibuprofen dissolution rates than the non-treated and pure crystalline drug. In case of PEG 6000, it should be noted that, the drug dissolution rate increases with increasing PEG 6000 weight fraction in the coprecipitates. Many investigators[18-20] have explained the increase in the dissolution rate in case of PEG 6000 and dextrose, as being due to the presence of drug in highly fine dispersed form. These carriers are expected to form interstitial solid solution with the drug , as well as retard its crystallisation due to slow migration and difficulty in nucleation. This would result in the formation of extremely fine particles of pure drug in freely soluble carriers. Also, the rapid dissolution may be attributed to the molecular and/or colloidal dispersion of drug in the carrier matrix.

The enhancement of the drug release in presence of non-ionic surfactants was explained on the basis of their surface activity, which increases the wettability of the hydrophobic surface of the drug, and thereby, increases the dissolution rate[21]. The fast release in cases of drug-surfactants coprecipitates is also in accordance with the findings of Chiou et al[22] and Chiou and Riegelman[23]. The expected defect in the

particle or crystal structure due to the formation of solid solution of water soluble surfactants in the drug particle or crystal brought about this increment in dissolution rate.

As we have mentioned before, the coprecipitation of Ibuprofen with non-ionic surfactants and water soluble carriers increased the amount of drug released.

These can be arranged as follows:
Tween 20 > Myrj 53 > PEG 6000 > Tween 80 > Dextrose.
The increase in dissolution rate was found to be concentration dependent (Table 1). Relative dissolution rate data (Table 1) is claculated by determining the amount of Ibuprofen dissolved for a particular sample divided by the amount of Ibuprofen dissolved from the untreated sample at the same time interval[24]. The maximum dissolution rate has been shown by using Tween 20 and Myrj 53 while PEG 6000 and Tween 80 followed by dextrose produced lower dissolution rates. These findings were proved by determining the time for 80 and 90% drug release (Table 2),While Tween 20 shows a 7.5 min. for 90% release, dextrose shows 32.5 min. It is worthy to mention that t_{80} and t_{90} for the drug alone were 55 and 71 min respectively.

The U.V. spectra of Ibuprofen-Coprecipitates showed no change in λ_{max} (222 nm) of Ibuprofen spectrum.

I.R. spectra showed that, there are no changes appear on the major peaks of Ibuprofen at 779, 1185, 1232, 1384 and 1721 cm^{-1}.

T.L.C. studies, revealed that, the coprecipitates were resolved into one spot with R_f value equal to that of Ibuprofen alone (0.67).

These results indicated that, there is no evidence of complexation between Ibuprofen and any of the selected additives.

In conclusion, the coprecipitation of drug with hydrophilic surface active agents enhanced its dissolution rate withount significant increase in the bulkness of its dose, while the use of water soluble carriers increased the bulkness of the drug, this would produce difficults in drug manufacturing.

Table 1: Relative dissolution rate of Ibuprofen at different concentrations of the additives.

Type of Additive	*Conc. w/w %*	*Relative Dissolution Rate at* * *2 min*	*5 min*	*10 min*
Tween 20	2.5	1.57	1.67	1.50
	5.0	2.00	2.00	1.75
	10.0	3.24	2.78	2.25
Myrj 53	2.5	1.57	1.55	1.42
	5.0	1.93	2.00	1.71
	10.0	2.86	2.50	2.13
Tween 80	2.5	1.30	1.44	1.25
	5.0	1.71	1.67	1.58
	10.0	2.57	2.30	2.00
PEG 6000	(2:1)	1.50	1.50	1.38
	(1:1)	2.00	2.00	1.88
	(1:2)	2.73	2.44	2.04
Anhydrous dextrose	(2:1)	1.28	1.22	1.13
	(1:1)	1.50	1.39	1.38
	(1:2)	1.71	1.67	1.50

* Relative D.R.= Amount of drug dissoluted from the treated samples

Amount of drug dissoluted from the untreated samples.

Table 2: Summarized data relevant to t_{80} and t_{90} of Ibuprofen alone and alcoholic-treated. Also, for the drug-soluble carrier* and drug-surfactants coprecipitates*

Type	$t_{80\%}$ *(min.)*	$t_{90\%}$ *(min.)*
Control (drug alone)	55	71
Alcoholic drug treated	55	71
Tween 20	2.5	7.5
Myrj 53	6.5	11.5
PEG 6000	7.5	12.5
Tween 80	9.0	17.5
Dextrose	20.0	32.5

* Higher concentration for the additives was used.

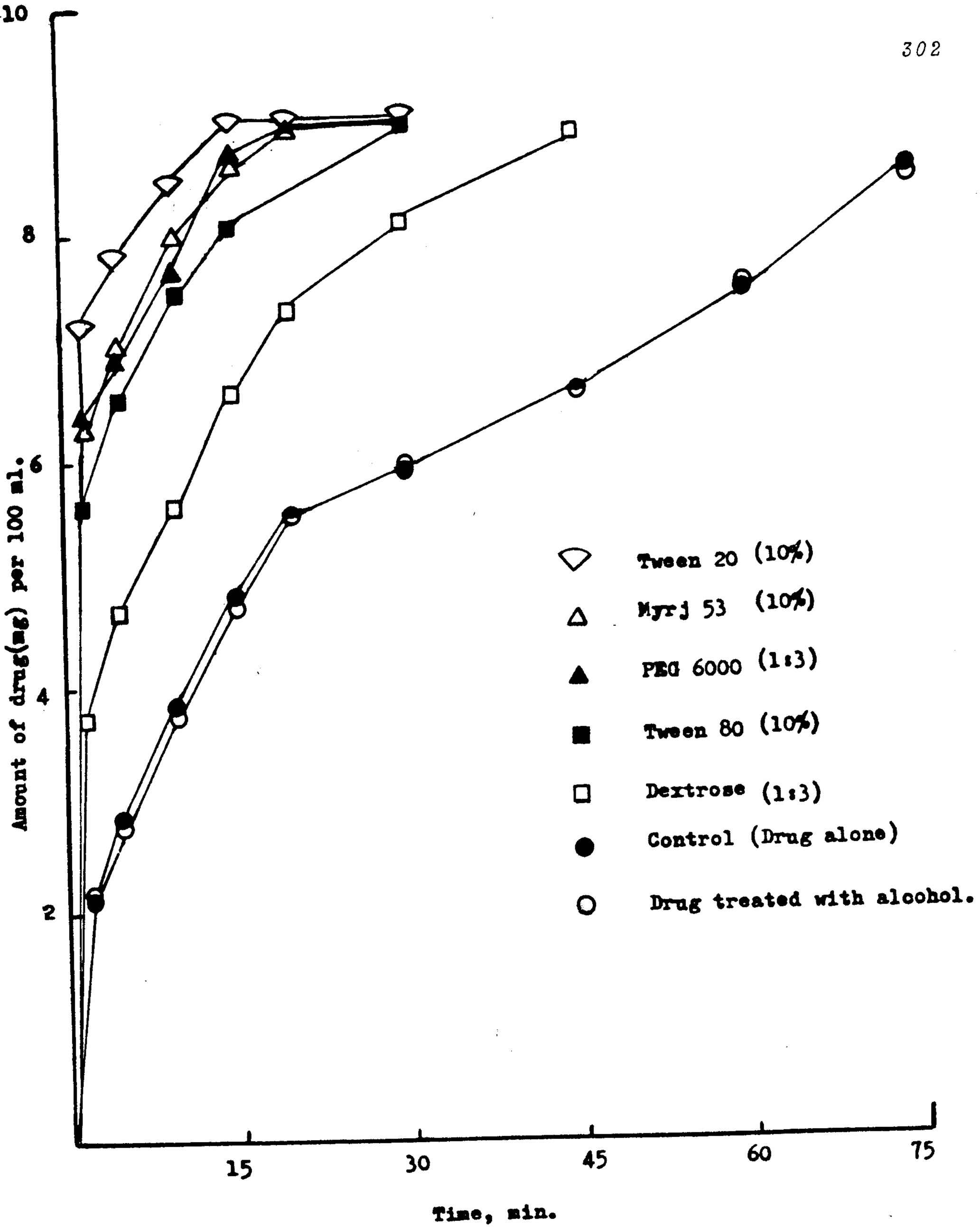

Fig. 1: Dissolution Profiles of Ibuprofen and Ibuprofen-Coprecipitates.

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اســـــراع الأذابه لمادة ابوبروفين باســـــعمال منشطات السطح والحامل الذى يـــذوب فى المـــــــــاء

محمد الشابورى ـ أحمد طلعت نـوح ـ عبد الجـــواد حلمـــــــــــــى
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درس تأثير منشطات السطح غير المتأينه وكذلك عديد الأيثلين جليكـــــول ٦٠٠٠ الجلوكوز كحاملات تذوب فى الماء على اسراع الأذابه لعقار الأيوبروفيـــن شحيح الذوبان فى المـــــاء .

ولقد وجد أن منشطات السطح أحدثت معدل اتاحة أفضل من عديد الأيثليـــن جليكول ٦٠٠٠ والجلوكوز وذلك فى النسب التى درســـت .

ولقد أوضحت كروماتوجرافيا الطبقه الرقيقه وكذلك الأشعة فوق الحمـــراء أى تفاعل حدث بين العقار والمواد المضافه . كما أن مقدار جر م العقـــار لايتأثر بكميه منشطات الســـطح المضافه كما وجد فى حالة الجلوكوز وعديـــد الأيثلين جليكول ٦٠٠٠ .

received in 24/11/1983 & accepted in 19/4/1984