THE EFFECT OF SURFACTANT ON THE DISSOLUTION RATE OF IBUPROFEN TABLETS

Nighat Razvi, Saeed Ahmad Siddiqui and Lubna Ghazal Khan *Department of Pharmaceutics, Faculty of Pharmacy, University of Karachi, Karachi-75270, Pakistan*

ABSTRACT: The present work was conducted on the effect of surfactant on the dissolution rate of ibuprofen tablets. The cationic (Cetyl Trimethyl bromide) and anionic (Sodium dodecyl sulphate) surfactant present in the dissolution media have remarkable effect on the dissolution rate of Ibuprofen. Maximum dissolution was obtained in the presence of anionic surfactant (Sodium dodecyl sulphate) at 0.5% concentration of de-ionized water whereas non-ionic (Tween-80) surfactant had little effect on the dissolution of Ibuprofen tablets.

KEY WORDS: Dissolution, Dissolution media, Sodium Dodecyl Sulphate, Cetyl Trimethyl Bromide, Tween-80, Dissolution rate.

INTRODUCTION

The oral administration is the most frequently used route for drug administration and usually intended for systemic effects resulting from drug absorption through the various mucosa of gastrointestinal tract. In current formulations, the oral dosage forms are tablets, must have disintegrate after contact with body fluid, and reach into the blood stream.

Since a drug must normally be in solution before absorption can take place, drug gives via orally administered tablets must dissolve in the contents of the gastrointestinal tract before systemic absorption can occur. Often the rate of drug absorption is determined by the rate of dissolution from the tablet.

Dissolution provides valuable information about bioavailability of the drug. It is considered to be one of the most important quality control tests performed on pharmaceutical dosage form. For drugs that are absorbed in the upper part of the gastrointestinal tract, i.e. acidic drugs, rapid dissolution is important.

The present study provided a fast and inexpensive method that correlates with the performance of dosage form in human body.

The improved oral absorption of drugs when administered with surface-active agents has been attributed to the improved solubility and dissolution rates due to solubility and/or wetting effects of the surfactants (Felmeister, 1972; Gander, *et ai.*, 1985).

The presence of surface-active agents in the dissolution medium has also been investigated. (Finholt & Solvang, 1968; Levy & Gumtow, 1963; Weintraub & Gibaldi, 1969) that at levels of surfactants below the critical micelle concentration, the principal effect involved would be a wetting phenomenon rather than solubilization, according to Finholt and Solvang (1968). These workers used phenacetin as the model hydrophobic drug and studied the dissolution rate of phenacetin in 0.1 N HCI containing different amounts of polysorbate-80. Other investigators have shown improved dissolution rates at levels of surfactants below the CMC. (Lim and Chen, 1974) reported that at pH 2.4 and 37°C, the apparent solubility of aspirin increased 17% in solution of cetylpyridinium chloride above its CMC (0.2%). However, at concentrations below CMC, dissolution rate and apparent solubility of aspirin decreased. Chiou *et at.*, (1976) enhanced the dissolution rates of sulfathiazole, prednisone, and chloramphenicol by re-crystallization of the drugs in aqueous polysorbate-80 solution.

Elworthy and Lipscomb (1968) substantiated these results by reporting that at high concentrations of surfactant, the viscosities of dissolution medium were enhanced markedly, decreasing the dissolution rate of griseofulvin.

Measurable enhancement in the dissolution rate of salicylic acid from an inert matrix was reported by Singh and co-workers when the contact angle "0" was lowered from 92° (water) to 31° (using 0.01 % dioctly sodium Sulfosuccinate. The surface tension also was correspondingly lowered from 60 to 31 dynes/cm. The similar findings were obtained in benzocaine studies when non-ionic surface-active agent i.e. polysorbate80 was used.

Pandit *et at.* (1985) proposed the use of surfactant solution as media for the dissolution testing of a

Apparatus	ERWEKA DT 6 Heusenstamm GMbh
Dissolution Medium	• 0.1 & 0.5% CTAB in Phosphate Buffer pH 7.2 • 0.1 & 0.5% CTAB in De-ioinized Water • 0.01 & 0.1% Tween-80 in Phosphate Buffer pH 7.2 • 0.01 & 0.1% Tween-80in De-ioinized Water • 0.1 & 0.5% SDS in Phosphate Buffer pH 7.2 • 0.1 & 0.5% SDS in De-ioinized Water
Volume	900 ml
Rotation speed	100 rpm
Temperature	37 ^{O}C ± 0.5 ^{O}C

Table 1: Comparative study of surfactant Effect on dissolution media for the dissolution rate of Ibuprofen at 100rpm paddle speed

Dissolution Media	Time In Minutes					
	10	20	30	40	50	60
Phosphate Buffer pH 7.2	91.26	93.22	97.01	98.59	98.49	102.51
Deionized Water (pH 7.0)	10.18	17.17	23.89	22.49	29.84	30.08
0.5% CTAB in Deionized Water	56.13	89.3	94.32	85.99	87.62	89.3
0.5% CTAB in Phosphate Buffer pH 7.2	66.46	71.88	73.1	78.87	91.27	94.58
0.1% CTAB in Deionized Water	32.12	45.13	52.09	58.36	66.8	69.79
0.1% CTAB in Phosphate Buffer pH 7.2	364.51	156.62	226.86	121.88	256.08	144.78
0.1% Tween-80 in Deionized Water	-43.69	-43.69	-43.69	-43.69	-43.69	-43.69
0.1% Tween-80 in Phosphate Buffer pH 7.2	-84.12	-84.12	-84.12	-84.12	-84.12	-84.12
0.01% Tween-80 in Deionized Water	14.04	19.13	24.25	28.28	32.26	35.22
0.01% Tween-80 in Phosphate Buffer pH 7.2	87.19	98.92	104.39	107.09	104.2	95.28
0.5% SDS in Deionized Water	40.42	62.29	90.8	92.08	96.84	97.61
0.5% SDS in Phosphate Buffer pH 7.2	60.69	84.89	100.8	62.77	70.9	75.63
0.1% SDS in Deionized Water	40.38	64.61	88.42	89.78	92.54	94.32
0.1% SDS in Phosphate Buffer pH 7.2	93.09	92.9	106.83	112.62	107.3	118.4

** Each reading is the mean of 3 readings.

poorly-water soluble drug. The solubility of 4-(4-biphenyly)-butanol was dramatically enhanced in the presence of cationic, anionic and even a non-ionic surfactants.

Other studies conducted on conventional formulation and capsule are also showed significant enhancement in the dissolution rate of poorly soluble drugs when surfactants were added to the dissolution medium, even at a level below the critical micelle concentration, probably by reducing the interfacial tension. Low levels of surfactants were recommended to be included in the dissolution medium as this seemed to give a better correlation b/w the *in vitro* data and in vivo condition.

Finholt and Solvang (1970) compared the dissolution behavior of phenacetin and phenobarbital tablets human gastric juice to that in dilute hydrochloric acid with or without various amounts of polysorbate-80 in the dissolution medium. The data showed that both pH and surface tension had significant influence on the

002-05/IICPMJ©Karachi University Press

dissolution kinetics of the drug studies. For example, they found that not only was the dissolution rate much faster in diluted gastric juice, but the rate increased with decreasing particle size, whereas the opposite was trace when O.lN HCI was used.

image

The presence of surface-active agents in the dissolution medium promotes wetting of the solute particles and enhances the dissolution rate, even if the concentration of the surfactant is below the CMC. This is extremely important for particles of irregular shapes with pores and cervices (Finholt & Solvang, 1970).

MA TERIALS AND METHODS

Different solution of cetyl trimethyl ammonium bromide (CTAB), Sodium dodecyl sulphate and Tween-80 were prepared in aqueous media and in phosphate buffer at pH 7.2.

General Procedure:

- 900mi of the dissolution medium were poured in each vessely. The dissolution medium was heated to 37°C :t 0.5°C. Lowering the paddle of the instrument to its required length, before rotation the vessel was covered to prevent the vaporization of the medium.

- The rotation speed of the basket was adjusted to 100 rpm at every time for each med\a. When temperature reaches to 37°C :t 0.5°C, one tablet was placed in each vessel and the stopwatch was started.

- Twenty (20) mL of sample were withdrawn after 10, 20, 30, 40, 50 and 60 minutes interval from different vessels. Then the sample was filtered. through Whattman filter paper (No. 41). Ten (10) mL of the filtrate was taken and diluted with the dissolution media up to 100 mL. Then 30 ml of the solution was taken and dilute with the same media to 100 mL.

Blank solution:

- Dissolution media was used as blank solution in the analysis.

Standard Solution:

- Twenty two decimal two (22.2) mg of Ibuprofen was weighed in 50 ml volumetric flask; 5 ml of methanol was then added to dissolve properly and then the volume was adjusted to 50 ml with the dissolution media.
- Ten (10) ml of this solution was pipette out and dilute with the dissolution media to 100 mL. Again 30 mL was pipette out and dilute with the dissolution media to make exactly 100 mL.

Measurement of Absorbance: The absorbance of the standard was taken and sample solution' at 221 nm spectrophotometer. using UV!Visible

Calculation:

$$\% \text{ Rate of Dissolution} = \frac{\text{Absorbance of sample} \times \text{Weight of Standard}}{\text{Absorbance of standard} \times \text{Weight of Ibuprofen in 1 tablet}} \times 100$$

Methodology:

The experimental conditions for the tablets dissolution tests are summarized in chart.

RESULTS AND DISCUSSION

Table 1 indicated that the dissolution rate of the Ibuprofen tablets increased when the surfactant added in the de-ionized water, while either their reduction or very little change in the dissolution wh'en surfactant added in the buffer solution pH 7.2.

The dissolution rate of the drug was increased when anionic surface-active agent added in the de-ionized water, while moderate to good results were observed with the addition of cationic surface-active agent. Non-ionic surface-active agent either showed retarding effect or very slight change in the dissolution rate when added in the water.

The dissolution rate of the drug increased when cationic surface-active agent added in the water at a concentration of 0.1 %. The rate was further increased as the concentration of the surface-active agent increased to 0.5%. This was due to the fact that the compound Ibuprofen was water insoluble and as the surface-active agent added in the system, it increased the wetting ability of the compound 'and thereby increased the solubility of the drug. As the concentration of the CT AB increased, the solubilization of the drug compound was also increased, resulting in an increase in the dissolution

rate of the drug. Lim and Chen, 1974 reported that the solubility of aspirin increased 17% in solution of cetylpyridinum chloride above its CMC. Similar results were reported by (Beckett & Quanch, 1996). This statement supports our result as the solubility of the Ibuprofen was also increased with the addition of CTAB above its CMC.

While on the other hand, when CT AB was added in water at 0.1 % concentration it showed unreliable results that might be due to the fact that the surfactant itself gives some response at the same wavelength. But when CT ABadded in 0.5% it showed decreased results as compare to obtain with phosphate buffer, pH 7.2. This might be due to the fact and (Katsumi & Ogawa, 1996) studies that at high concentration of surfactant the viscosity of the dissolution media increased, decreased the dissolution rate of the drug.

Table 1 showed when nonionic surface-active agent i.e. Tween 80 in 0.01 % concentration was used in the dissolution media it showed only slight increase in the dissolution of Ibuprofen, this might be due to the fact that 0.01 % can only increases the wetting capacity of the drug rather than solubilization. Moore, 1996 also revels that at levels of surfactants below the CMC, the principal effect involved would be a wetting phenomenon rather than solubilization.

At a concentration of 0.1 % Tween-80 in dissolution medium, the result were found unsatisfactory and this was might be due the fact that at high concentration the dissolution media would become very viscous and did not allow the drug compound to dissolve in the dissolution media (Table 1).

Fig. 1 indicated that the dissolution of Ibuprofen increases with the addition of anionic surfactant. When sodium dodecyl sulphate used in a concentration of 0.5%, it provides excellent results of dissolution that might be due to the fact that it increases both the wetting capacity and the solubilization of the drug in the dissolution media. In the presence of phosphate buffer, pH 7.2, the dissolution results obtained, were not reliable, as an early increase in the dissolution observed. This is due to the fact and reported by Chakarbarti & Marylee, 1997 that when the surfactant reaches above its CMC level it could only influence the solubilization of the drug and could not affect the wetting capacity of the drug, which results in an early increase in the absorption of the drug.

REFERENCES

Beckett, A.H., and Quanch, T.T. Dissolution Technologies, 3(2): 7-10 (1996).

Chakrabarti, S., and Marylee, Z.S. 1. Phar. Sci. 86(4): 465 469 (1997).

Chiou, W.L., Chen, SJ. and Athanikar, N., J. Pharm. Sci. 65: 1702 (1976).

Elworthy, P.H. and Lipscomb, F.J., 1. Ph arm. Pharmacol., 20: 923 (1968). Finholt, P. and Solvang, S., J. Pharm. Sci. 57: 1322 (1968). Gander, B., Ventouras, K., Gurny, R., and Doelker, E. Int. J. Pharm. 27: 117-124 (1985).

Gharbo, S.A., Congnoin, M.M., and Williamson, MJ., Drug Dev. Ind. Pharm. 15:331-335 (1989).

Katsumi Iga and Yasuaki Ogaawa. Takeda Kenkyushoho. 55: 173-187 (1996).

Levy, G. and Gumtow.,R.H., J. Pharm. Sci. 52: 1139 (1963).

Lim, J. K. and Chen, c.c., 1. Pharm. Sci. 63: 559 (1974).

Moore, T.W. Dissolution Technologies. 3(2): 3-5 (1996).

Pandit, N.K., Strykowski, J.M., McNally, EJ., and Waldbilling,A.M., Drug Develop. Indust. Pharm., 11 (10&9): 179 (1985).

Robert C. Wojcik. Dissolution Technologies. 4(3): 12-20 (1997).

Solvang, S., Finholt, P. J. Pharm. Sci. 59: 49 (1970).

Weintraub, H. and Gibaldi, M., J. Pharm. Sci. 69:1368 (1969).

Manuscript received 05 - 10 - 2004
Accepted for publication 04 - 12 - 2004