Online Available at www.thepharmaresearch.info

THE PHARMA RESEARCH

AN INTERNATIONAL JOURNAL

The Pharma Research (T. Ph. Res.), (2012), 6(2); 14-18. 0975-8216; Copyright © 2012 by Sudarshan Publication

DISSOLUTION OF BENZOIC ACID USING MIXED HYDROTROPES

Ch.V.Subbarao[1], P.Suresh[1] and Ch.Siva Prasad[1]

Affiliated to:

[1]Department of Chemical Engineering, MVGR College of Engineering, Chintalavalasa, Vizianagaram-535005, Andhra Pradesh, India.

ABSTRACT

Experiments are performed for dissolution of Benzoic acid (a widely used antifungal and antibacterial and poorly water-soluble drug) in presence of hydrotropes in the concentration range of 0.05N to 2N. The hydrotropes used in the present study are urea, trisodium citrate and mixture of urea and trisodium Citrate. Not much improvement in the solubility of Benzoic acid in presence of urea hydrotrope is observed. In case of Trisodium citrate, the minimum hydrotrope concentration (MHC) and Maximum concentration (C_{max}) are found to be 0.05N and 1.5 N respectively. In case of mixed hydrotropes consisting of urea and trisodium citrate, solutions of same normality are mixed at different volume ratios. It has been observed that MHC and C_{max} for mixed hydrotropes are not significantly different from trisodium citrate hydrotrope alone. Not much increase in the solubility is observed in case of hydrotrope mixture compared to trisodium citrate hydrotrope indicating that hydrotropes need not always yield high solubility than individual hydrotrope.

Keywords: Drug, hydrotrope, MHC, C_{max}, volume ratio

INTRODUCTION

It is well recognized that the dissolution rate can be the limiting step in the biological availability of drugs administered in solid state. Literature reports the relation of dissolution rate to biological availability [1]. The factors influencing the dissolution rate were reviewed by some researchers [2]. Models were for dissolution rate are also reported in the literature [3].

Benzoic acid is used as a perfume intermediate, dye intermediate, cosmetic flavoring, and preservative. Enhancing the aqueous solubility of benzoic acid and others is of interest because of the challenges in extracting them due to the extremely low

aqueous solubility of these acids. The dissolution rates of Benzoic acid (which is sparingly soluble in water) was reported using phosphate buffer [4], tyloxal, polysorbate 80, sodium lauryl sulfate and polyoxol surfactants [5]. Works were also reported for its dissolution in aqueous solutions of Carboxy methyl Cellulose (CMC) [6] and in aqueous solutions of ethanol and N-proponal [7]. Literature available is sparse on its dissolution using hydrotropes.

Hydrotropes are class of compounds that affect a several fold increase in the solubility of sparingly soluble solute under normal conditions. The origin of hydrotropy dates back to 1916 when Neuberg identified that this pioneering technique for effecting very large solubility enhancement for variety of sparingly soluble compounds [8]. Hydrotropes are in general water-soluble and surface-active compounds which can significantly enhance the solubility of organic solutes. They are extensively used for dissolution of various water insoluble drugs as reported in the review of drug solubilization [9]. Literature reports standardization of methods using hydrotropy and their comparison with I.P method [10].

Present study is aimed at increasing its solubility using Urea and Tri-sodium citrate as hydrotropes. Experiments are also performed by mixed solutions of both the hydrotropes at various volume ratios since it is reported that mixed hydrotropes are reported to increase the solubility compared to individual hydrotropes [11].

Experimental procedure:

Urea solution of 0.05 M is prepared by dissolving required quantity of urea in $1X10^{-3}$ m^3 in carbon dioxide free distilled water. 50ml of this solution is taken and to this excess of benzoic acid is added.

The procedure mentioned above is repeated while preparing Trisodium citrate solutions of different concentrations.

The experiments and analysis are carried out as per the procedure recommended by Maheswari et al [10].

While preparing mixed hydrotropes of urea (U) and tri-sodium citrate (T) , same Molarities of urea and tri-sodium citrate (0.1, 0.3, 0.5, 0.8, 1, 1.5, 2) are mixed at different volume ratios. 45:5 (volume ratio 9) ratio is prepared by mixing 45ml of urea with 5ml of Trisodium citrate (both at the same molarity). 4, 1.5, 2/3, 1/4, 1/9 volume ratios of U:T are prepared for carrying out experiments.

Results and Discussion:

Variation of solubility of Benzoic acid with urea concentration: The following plot (Fig.1) gives variation of solubility of benzoic acid with urea concentration.

It can be seen from the plot that the solubility of benzoic acid in water yielded only 0.028M (i.e 3.4g/l).

It can be concluded that not all hydrotropes increase the solubility of sparingly solid.

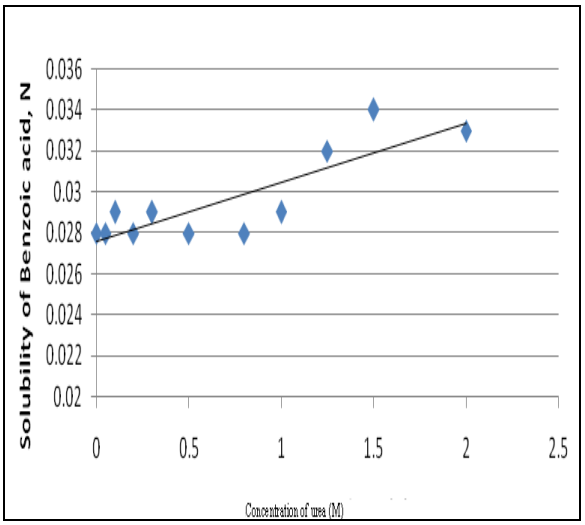

Fig.1: Effect of Urea concentration on solubility of Benzoic acid

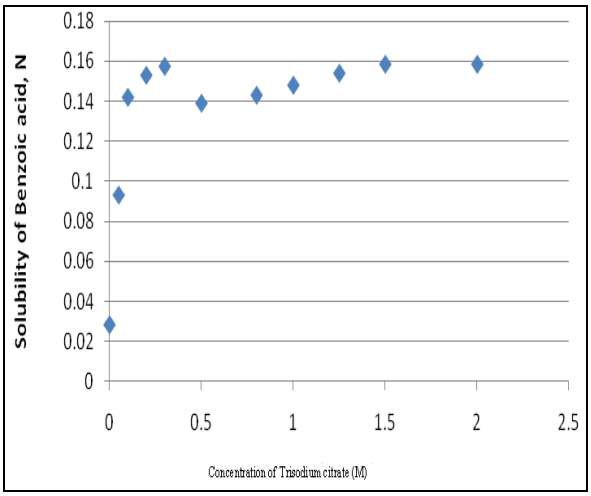

Fig.2: Effect of Tri-sodium citrate concentration on solubility of Benzoic acid

Variation of solubility of Benzoic acid with tri-sodium citrate concentration:

The following plot (Fig.2) gives variation of solubility of benzoic acid with tri-sodium citrate concentration.

The plot suggests that there is a remarkable improvement in the dissolution of benzoic acid when Tri-sodium citrate is used as hydrotrope.

The plot also suggests a minimum hydrotrope concentration (MHC) of 0.01M and solubility at MHC is 0.09M and a maximum limit to the solubility is achieved at 1.5M where the solubility of benzoic acid is 0.16M. This is known as C_{max} (Maximum concentration beyond which there in no further increase in solubility).

Table-1: Variation of solubility of benzoic acid with respect to normality mixed hydrotropes and different volume ratios of hydrotropes.

(/U/T)/ Normality of mixed solution	0.05M	0.1M	0.2M	0.3M	0.5M	0.8M	1M	1.25M	1.5M	2M
9	0.034	0.05	0.06	0.08	0.08	0.08	0.09	0.11	0.12	0.12
4	0.036	0.06	0.11	0.10	0.10	0.11	0.112	0.13	0.15	0.15
1.5	0.059	0.09	0.08	0.12	0.13	0.13	0.147	0.15	0.16	0.16
0.66	0.066	0.11	0.13	0.13	0.13	0.13	0.148	0.15	0.16	0.16
0.25	0.086	0.13	0.14	0.15	0.13	0.14	0.142	0.14	0.16	0.16
0.11	0.091	0.14	0.15	0.152	0.14	0.14	0.145	0.15	0.16	0.16

Variation of Solubility of Benzoic acid for different volume ratios of Urea/Trisodium citrate:

The following table (Table-1) gives the MHC and Cmax details for different volume ratios of mixed hydrotropes**.** (U/T represents volume ratio of Urea to Trisodium Citrate).

It can be concluded from the table that MHC for all the volume ratios is at 0.05M and Cmax occurs at 1.5M. No increase in solubility is observed when mixed hydrotropes are used. It can be concluded from the table that the maximum solubility of 0.16M in case of mixed solutions is obtained for a U/T ratio of 0.66 and mixed solutions concentration of 1.5M.

The data also suggests that mixing of hydrotropes need not always lead to increase in solubility.

CONCLUSIONS: Some of the conclusions of the above study are

1. Not much improvement in solubility of benzoic acid is observed when urea is used as hydrotrope.
2. Tri-sodium citrate increased the solubility of Benzoic acid with a MHC of 0.05Mand Cmax at 1.5M
3. Mixed hydrotropes need not always increase the solubility of sparingly soluble solid when compared to individual hydrotropes.

ACKNOWLEDGEMENTS:

The authors are thankful to the Principal Dr. K.V.L.Raju and the management of MVGR College of Engineering, Vizianagaram for providing the necessary infrastructural facilities. The authors are also thankful to the head of the department of Chemical Engineering, Andhra University for providing the necessary support. The authors would like to thank Professor Ch. Durga Prasada Rao for useful discussions.

REFERENCES:

1. Wagner,J.G, Biopharmaceutics :Absorption aspects, 1961;50, 359-387
2. Wurster, D.E and Taylor, P.W Dissolution rate, J.Pharm.sci 1965;54:169-175
3. Higuchi,W.I Diffusional model useful in pharmaceutical drug release process, J.Pharm.sci 1967;56:315-324
4. Ramtool, Z and Corrigan, O.I Dissolution characteristics of benzoic acid in reactive media, drug development and ind.phar.1987;13:1703-1720
5. Parrot, E.L and Sharma,V.K Dissolution kinetics of Benzoic acid in high concentrations of surface active agents, J.Pharm.sci, 1967 ;56:1341-1343.
6. Surendra Kumar, Siddh N. Upadhyay, and Virendra K. Mathur, On the Solubility of Benzoic Acid in Aqueous Carboxymethylcellulose Solutions, J. Chem. Eng.Data, 1978 ;23:139-141.
7. Ricardo F. Pires and Moilton R. Franco, Jr.Solubility of Benzoic Acid in Aqueous

Solutions Containing Ethanol or N-Propanol, *J. Chem. Eng. Data*, 2008; 53 :2704–2706

8. John, A. D. *Lange's Handbook of Chemistry*; McGraw-Hill, New York (1987).15th ed.347.
9. Subbarao, Ch.V., Manjeera, Ch, Swarna. P and Krishna Prasad,K.M.M, role of hydrotroeps in solubilizing drugs- a review, T.Phar.Res.2011; 6(1):48-59
10. Maheshwari Rajesh Kumar, Rajput Mithun Singh, Mathur Vineet, Satrawala Yamini, Gupta Amit , Quantitative estimation of Benzoic acid in bulk sampe using sodium benzoate and sodium salicylate as hydrotropic solubilizing agent, T. Pharm. Res., 2009;2: 1-7.
11. Rajesh Kumar Maheshwari, Arpna Indurkhya, application of mixed hydrotropic solubilization technique in the formulation and evaluation of hydrotropic solid dispersion of aceclofenac, Asian.J.Pharm.2010; 4: 235-238.
12. Rajesh k. Maheshwari, chanpreet juneja, nitin juneja, Application of mixed-hydrotropic solubilization concept in spectrophotometric analysis of frusemide in tablet dosage form, T. Ph. Res., 2010, 3; 243-248