RESEARCH NOTE

MISCIBILITY BEHAVIOUR OF BINARY MIXTURES OF BENZYL BENZOATE AND LIQUID PARAFFIN

F.A. OLADIMEJI[+] and L.O. ORAFIDIYA
Department of Pharmaceutics, Obafemi Awolowo University, Ile-Ife, Nigeria.

(*Submitted*: 04 February 2005; *Accepted*: 16 October 2006)

Abstract
Miscibility of binary mixtures of benzyl benzoate and liquid paraffin as functions of temperature and composition has been determined using phase separation method. The binary mixtures demonstrated a critical (upper) solution temperature of 35 °C at 101325 Nm^{-2} with a mixing gap. A tie-line drawn at 28 °C across the phase diagram indicated that benzyl benzoate at concentrations between 38% and 77% remained practically immiscible with liquid paraffin due to phase saturation, while phase separation will occur in a solution containing a binary mixture of 25% benzyl benzoate in liquid paraffin stored at temperatures lower than 18 °C.

Keywords: Benzyl benzoate, liquid paraffin, binary mixtures, temperature-composition miscibility, phase diagram.

1. Introduction

A comparative preliminary clinical test of leaf essential oil of *Lippia multiflora* Moldenke, family Verbenaceae (*Lippia* oil) and benzyl benzoate as ectoparasitic agents was carried out using liquid paraffin as the placebo and diluting medium (Oladimeji *et al*., 2000). The choice of liquid paraffin as diluting medium arose from the fact that it is stable, non-reactive (Turkoglu *et al*., 1999), and non-sensitizing (Fisher *et al*., 1971). However, while the *Lippia* oil was completely miscible with the liquid paraffin at all concentrations, benzyl benzoate exhibited concentration dependent miscibility in liquid paraffin, thus limiting the concentration at which the benzyl benzoate could be applied for the clinical test. The degree of miscibility of two liquids is often dependent on temperature and their composite concentrations (Peters *et al*., 1992; Lim *et al*., 1993). Partially miscible liquids are generally categorized into three different systems based on increased miscibility with rise in temperature (Eustaquio-Rincon *et al*., 1993; Cuevas *et al*., 1995), decreased miscibility with rise in temperature (Chen *et al*., 1997), and miscibility showing upper and lower temperature dependence (Gelb *et al*., 1999; Foreman and Luks, 2000). The degree of solubility or miscibility of benzyl benzoate with some liquid media has been reported (Reynolds, 1989). However, there is no report on the miscibility of binary mixtures of benzyl benzoate and liquid paraffin. In this study, the effect of temperature and composition variations on the degree of miscibility of binary mixtures of benzyl benzoate and liquid paraffin is investigated and reported.

2. Experimental

Benzyl benzoate and light liquid paraffin (Williams Ransome and Sons Ltd., England), whose weight per milliliter (g/mL) were determined as 1.1131 ± 0.0081 and 0.8397 ± 0.0057, respectively, using British Pharmacopoeia method (1998) were used for the experiment. A series of binary mixtures of varied concentrations of benzyl benzoate (5 to 95%) in liquid paraffin were prepared volumetrically in 10ml stopper measuring glass cylinders graduated in 0.1 mL. The required volume of the benzyl benzoate was added to the liquid paraffin and shaken for 5 min using a mechanical shaker. The test samples were stored at appropriate temperature (6 to 45 °C) ± 0.5 °C over a period of 24h in thermo-regulated refrigerator (Astell Hearson, England) or water bath (GFL, Germany). The samples were subsequently observed for total miscibility or phase separation (Lim *et al*., 1993). The temperatures at which the two liquids become miscible were recorded, while the volume fraction of the separated phases at different temperatures and concentrations were measured. The results were the mean values ± SD of three determinations for each of the twenty treatments. The experimental results and the calculated values were subjected to *t*-test with minimum level of significance established at 5% (Steel and Torrie, 1980).

+ *corresponding author* (email:faolad@oauife.edu.ng)

3. Results and Discussion

The temperature-composition phase diagram of binary mixtures of benzyl benzoate and liquid paraffin is indicated in Fig. 1. The mixtures fall into category of a system showing increase in miscibility with rise in temperature. The phase boundary points AB and CD represent the effect of temperature on the miscibility of benzyl benzoate in liquid paraffin and that of liquid paraffin in benzyl benzoate, respectively. To the right of line AB, addition of benzyl benzoate to liquid paraffin led to separation into two phases to give a saturated solution of benzyl benzoate in liquid paraffin until line CD is reached. Further addition of benzyl benzoate to liquid paraffin after line CD, led to the formation of an unsaturated solution of liquid paraffin in benzyl benzoate as a single phase. The phase boundary curve ABCD, therefore, separates the single-phase system of one liquid (solution of benzyl benzoate and liquid paraffin) from a two-phase system of two mutually saturated liquids. Above line BC, which has been defined as Critical (upper) Solution Temperature (CST) (Cuevas *et al.*, 1995; Gelb *et al.*, 1999), the benzyl benzoate and the liquid paraffin were miscible in all proportions. This critical upper solution temperature was found to be 35 °C for the binary mixture of benzyl benzoate and liquid paraffin. The phase boundary points AB and CD were further regressed and defined by equations

$2.65 + 0.53X$ ($r = 0.93$) and

$121.56 - 1.24X$ ($r = -0.99$), respectively,

from which the value of X (concentration of benzyl benzoate at CST) was calculated (tangent method) as 67.2% v/v, which is not quite different from 68.0% v/v obtained experimentally. The concentrations of benzyl benzoate at which miscibility with liquid paraffin will occur at temperature below 35 °C were calculated based on the two equations and the values compared statistically with those obtained experimentally. The calculated *t*-value (1.782) compared with the tabulated value (2.093, df = 19), indicated no significant difference between the calculated and experimental data ($P > 0.05$). A tie-line drawn at 28 °C (room temperature) across the phase diagram indicated that benzyl benzoate at concentrations between 38.0% and 77.0% v/v remained immiscible with liquid paraffin due to phase saturation. The miscibility of benzyl benzoate with liquid paraffin at concentration higher than 77.0% v/v, however, was due to formation of an unsaturated solution of liquid paraffin in the benzyl benzoate.

4. Conclusion

The effective concentrations of benzyl benzoate prescribed for the treatment of scabies range between 10% and 25% (Reynolds, 1989; Elgart, 1996; Olasode and Onayemi, 1998). While such concentrations are readily miscible with liquid paraffin at 28 °C (an average room temperature encounters in the tropics), it is implied from the phase diagram obtained in this study that a binary mixture containing 25% benzyl benzoate in liquid paraffin will separate at temperatures lower than 18 °C.

REFERENCES

British Pharmacopoeia, 1998. Her Majesty's Stationery Office, London. Appendix VG.

Chen, C.Y., Yunus, W.Z.W., Chiu, H.W. and Kyu, T., 1997. Phase separation behaviour in blends of isotactic polypropylene and ethylene-propylene diene terpolymer. *Polymer,* 38, 4433-4438.

Cuevas, R.M., Eustaquio-Rincon, R., Romero-Martinez, A. and Arturo, T., 1995. Experimental liquid-liquid miscibility curves for binary systems: ethanenitrile and butanenitrile with n-alkanes. *Fluid Phase Equilibria,* 107, 201-212.

Elgart, M.L., 1996. A risk-benefit assessment of agents used in the treatment of scabies. *Drug Safety,* 14, 386-393.

Eustaquio-Rincon, R., Romero-Martinez, A. and Trejo, A., 1993. Liquid-liquid miscibility curves for binary sytems: N-methylpyrrolidone with several hydrocarbon isomers. *Fluid Phase Equilibria,* 99, 187-201.

Fisher, A.A., Pascher, F. and Kanof, N.B., 1971. Allergic contact dermatitis due to ingredients of vehicles. *Arch. Derm*., 104, 286-290.

Gelb, L.D., Gubbins, K.E., Radhakrishnan, R. and Sliwinska-Bartkowiak, M., 1999. Phase separation in confined systems. *Rep. Prog. Phys.*, 62, 1573-1659.

Foreman, C.M. and Luks, K.D., 2000. Partial miscibility behaviour of the ternary mixture of carbon dioxide + n-tetradecane + acetone. *Fluid Phase Equilibria,* 169, 65-73.

Lim, K., Reckley, J.S. and Smith, D.H., 1993. Liquid-liquid phase equilibrium in binary mixtures of the nonionic amphiphile $CH_3(CH_2)_5(OCH_2CH_2)_2OH$ and water. *J. Colloid Interface Sci.*, 161, 465-470.

Oladimeji, F.A., Orafidiya, O.O., Ogunniyi, T.A.B. and Adewunmi, T.A., 2000. Pediculocidal and scabicidal properties of *Lippia multiflora* essential oil. *J. Ethnopharmacol.,* 72, 305-311.

Olasode, O.A. and Onayemi, O., 1998. Scabies: revisit in a depressed economy. *Central Afr. J. Med.,* 44, 18-21.

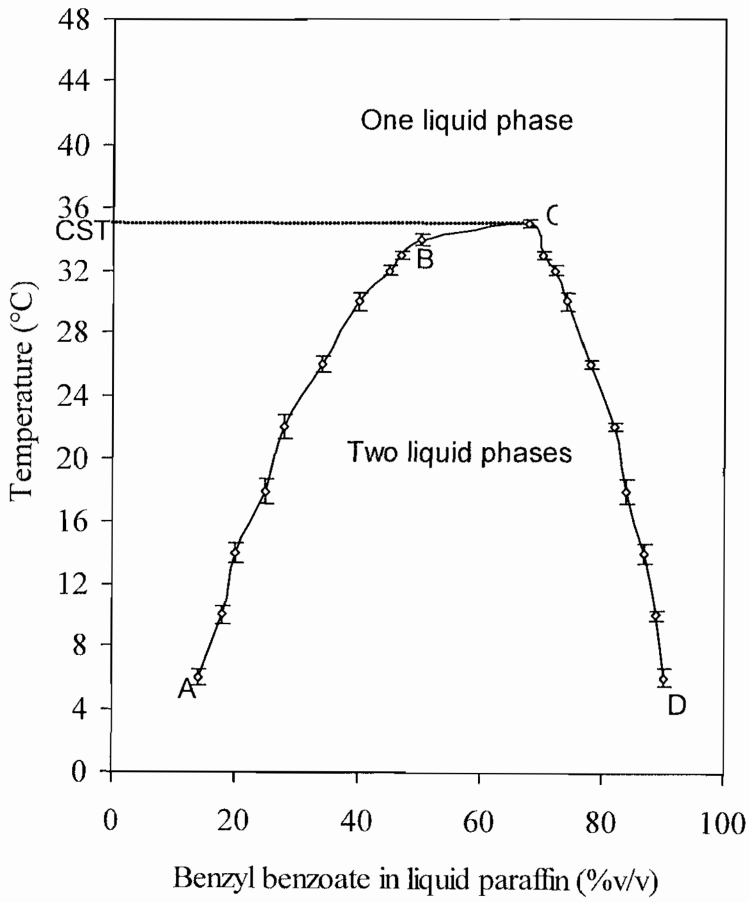
Peters, C.J., de Roo, J.L. and Arons, J.S., 1992. Measurements and calculations of phase equilibria in binary mixtures of propane + tetratriacortane. *Fluid Phase Equilibria,* 72, 251-266.

Reynolds, J.E.F., 1989. Martindale. The Extra Pharmacopoeia. (29th Ed.), The Pharmaceutical Press, London, 1345pp.

Steel, R. G. D. and Torrie, J. H., 1980. Principles and procedures of statistics. A biometrical approach (2nd Ed.), McGraw-hill Kogakusha, Ltd., Tokyo, 633pp.

Turkoglu, M., Pekmezci, E. and Sakr, A. 1999. Evaluation of irritant potential of surfactant mixtures. *Int. J. Cosmetic Sci.*, 21, 371-382.

Fig.1: Temperature-composition phase diagram of binary mixtures of benzyl benzoate and liquid paraffin.



Legend to Fig. 1:
CST = Critical Solution Temperature (35 °C).
ABCD = Phase boundary points.