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Microemulsion encapsulation of diospyrin, a plant-derived bisnaphthoquinonoid of potential chemotherapeutic activity

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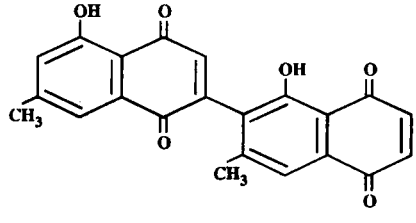
Diospyrin [**D1**], isolated from *Diospyros montana* Roxb., and some of its synthetic derivatives were found to possess significant antitumour (Hazra et al 1984) and antiprotozoal activities (Yardley et al 1996), thereby establishing it as a potential 'lead' compound to develop new chemotherapeutic agents against vector – borne tropical parasitic diseases. Compartmentalised liquids, eg. liposomes, micelles and microemulsions are increasingly being studied for efficient transport of drugs (Attwood & Florence 1983). Thus, designing a microemulsion vehicle for D1 and its analogues was envisaged in order to obtain a suitable drug-delivery system for these bioactive compounds with poor hydrophilicity. D1 was



Diospyrin [D1]

encapsulated in the clove oil droplets of "oil-in-water" microemulsion comprising clove oil – Tween 20 – water at a composition (5 : 30 : 65 w% ; 0.25 mg D1/ml of m/e) determined from the phase diagram (Gupta et al 1995; Mitra et al 1996). The encapsulated formulation was stable for at least three months. The spectral pattern of D1 [studied in Shimadzu UV-VIS 160A spectrophotometer] in ethanol solution was found to be altered in the compartmentalised medium, indicating an appreciable change in the microenvironment of the drug due to encapsulation. From the dynamic light scattering studies [Otsuka DLS 700, He-Ne Laser source at 632 nm] the drug – encapsulated droplets were found to be of slightly larger diameter (20.7 nm) as compared to the blank preparation (16.8 nm). Concomitant to the physical studies, *in vivo* bioassays against Ehrlich ascites carcinoma [EAC], a transplanted murine tumour, were undertaken [Table 1] to compare the

Table 1. Bioassay of Diospyrin – Free (T1) & Encapsulated (T2) – Against Ehrlich Ascites Carcinoma (E A C) in Swiss A Mice[a]

Group	Dose [Number] (mg/kg/day; i.p.)	M.S.T.[b] (No. of days)	I.L.S. (%)[c]
C	Nil	19.5	–
T1[d]	1.25 [8]	27.5	38
T2	1.25 [8]	36.5	87

[a]Challenge = 2 x 10^6 E A C cells per mouse i.p.
[b]M.S.T. = Median survival time
[c]I.L.S. = Increase in life span
[d]Dissolved in DMSO after maceration with Tween 80

antitumour activities of D1 in non-aqueous vehicle [T1] and D1 encapsulated in the microemulsion [T2]. Substantially greater increase in life span of 'T2' group than that for 'T1' group in relation to the control group 'C' was observed. The respective solvent vehicles showed no perceptible effect on the tumour growth parameters. Thus, the microemulsion vehicle was found to be an efficient carrier of the drug D1. Further studies are under progress to extend the application to other synthetic analogues in this novel series of potential bioactive compounds.

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