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# Oral administration of heat-solubilized curcumin for potentially increasing curcumin bioavailability in experimental animals

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Sir,

The paper by Narayanan *et al*., 20091 demonstrating the protective effect of curcumin and resveratrol in prostate cancer gives an interesting insight regarding the use of phytochemical combination therapy. It is of interest to note that liposome encapsulated curcumin was used for in vivo experimental animal use in this study to resolve the bioavailability issue of curcumin, resulting from poor absorption.1

It is very likely that poor absorption is a consequence of the fact that curcumin is practically insoluble in water. Therefore, solubility is an important issue in *in vitro* and *in vivo* experiments. Here, we would like to point out that we have shown increased solubility of curcumin (12-fold) and turmeric (3-fold) by the use of heat.2

The treatment with heat did not destroy curcumin's biological activity, as shown by its inhibition of 4-hydroxy-2-nonenal (HNE) mediated modification (80% inhibition of HNE-modification) of a multiple antigenic peptide3 substrate in an enzyme-linked immunosorbent assay4 that employed HNE-modification of a solid-phase antigen substrate. Mass-spectrometric (matrix assisted laser desorption ionization time of flight) and spectrophotometric (400-700 nm) analysis of curcumin solubilized by heat did not demonstrate any heat-mediated disintegration of curcumin.3،5 In addition, we have also shown that curcumin solubilized in mild alkali (pH 7.6, 130 μM) also significantly inhibited HNE-antigen modification.6 It has been shown that most of the curcumin (90%) in phosphate buffered sulfate and serum free media (pH 7.2, at 37°C) was broken down in 30 min.7 The treatment with heat, however, appears to protect curcumin from breaking down faster. Heat-solubilized curcumin amounts decreased 47% in 12 h compared to starting levels, and 67% in 72 h compared to starting levels.2

Curcumin (1,7-bis[4-hydroxy-3-methoxyphenyl]-1,6-heptadiene-3,5-dione) is the most active ingredient of turmeric obtained from the rhizome *Curcuma longa*.7 This yellow pigment is a polyphenol that has been shown to be efficaceous against a variety of diseases, including cancer.2،7–9

Several vehicles have been employed to deliver curcumin *in vivo* or topically. DMSO (dimethyl sulfoxide) has been used for curcumin administration *in vivo*.10 A combination of

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hydroxypropyl-beta-cyclodextrin and propylene glycol alginate have been found to be best with respect to solubility of curcumin and release from the vehicle11 for topical delivery of curcumin. Incorporation of curcumin in an oil-in-water microemulsion12 has also been used for topical application. Another group13 has shown the potential of poly(ethylene oxide)-b-poly(epsilon-caprolactone)micelles as an injectable formulation for efficient solubilization, stabilization, and controlled delivery of curcumin in *in vitro* studies. Kunwar *et al*.14 have attempted curcumin binding to albumin and the use of liposomes as vehicles to deliver curcumin to live cells.

For delivery of drugs *in vivo* or topically, water is indisputably the simplest and the most non-toxic vehicle, provided the drug is soluble in aqueous medium. We have already demonstrated a significant increase in solubility of curcumin in water. Here, we suggest the possibility of considering heat-solubilized curcumin15 for future *in vivo* and *in vitro* studies.

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