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Short Communications

Studies on curcumin and curcuminoids. X. The use of curcumin as a formulation aid to protect light-sensitive drugs in soft gelatin capsules

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The popularity of gelatin capsules as an alternative to compressed tablets as a solid dosage form has increased in recent years, largely due to the finding that this form of presentation has distinct advantages with respect to bioavailability. Also, the improved availability of capsule-filling machines with increased rate of output, together with the relatively high cost of formulating drugs as tablets, facilitates the economic justification for gelatin capsules. A wide range of liquids, solid suspensions and even some soft semisolids can now be incorporated into soft gelatin capsules on a commercial scale. The colour of the capsule shell is not without importance. At least 3 reasons are given for choosing coloured gelatin capsule shells when formulating a product. Firstly, there is evidence to suggest that colour is a factor in patient acceptability. Secondly, the colour of the capsules is important for identification of the product. Thirdly, coloured capsule shells offer protection to the contents from light. This is of great importance to the pharmaceutical industry and also to the hospital pharmacy where capsules are often dispensed into unit dose plastic containers and stored on open shelves in the pharmacy. The capsule content is then under continuous influence of light. Capsules are usually coloured by the use of synthetic dyes or inorganic pigments. Many countries have issued a ban on synthetic dyes in food and drugs, and the interest in natural colouring matters as a formulation aid in pharmaceutical preparations is increasing. The rhizomes of the plant, *Curcuma longa* L. (Zingiberaceae), contain 2–5% of a yellow compound, curcumin, and two related demethoxy compounds present in small amounts. The rhizomes and extracts of the rhizomes are commercial products used as colouring matter in food processing around the world (Tønnesen, 1986). Curcumin is a crystalline compound with a bright orange-yellow colour. Curcumin is substantially insoluble in water, which limits its use as a colour for systems containing a significant amount of water. A water-soluble curcumin complex suitable for use as a colouring agent in foods is, however, prepared by dissolving and mixing a source of curcumin and gelatin in an aqueous acid solution (Schranz, 1983). Further, it is known that curcumin has a stabilizing effect of certain photolabile drugs in solution and in topical preparations (Thoma, 1983).

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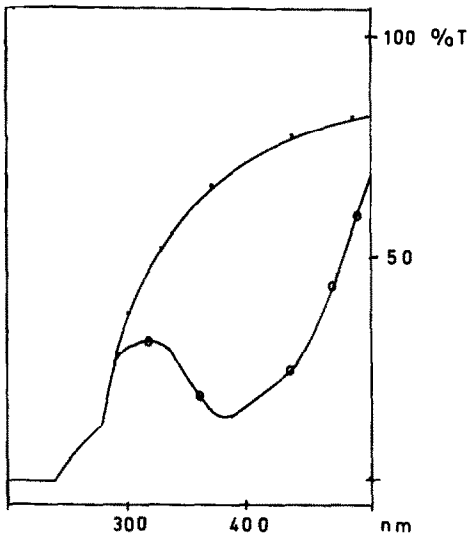

Fig. 1. Transmission spectrum of a plain gelatin capsule (■——■) and a gelatin capsule coloured with curcumin (○——○).

Curcumin was incorporated into soft gelatin capsule shells by making a curcumin–gelatin complex according to the method described by Schranz. Curcumin was mixed with a solution containing 20% water : 77% glacial acetic acid : 3% gelatin (w/w/w). The water was heated to about 40 °C to dissolve the gelatin, and the glacial acetic acid and curcumin were then added. Since commercially obtained curcumin contains a mixture of the 3 different naturally occurring isomeres, pure synthetic curcumin was chosen for these investigations (Tønnesen, 1986). The capsule shells investigated contained 0.02–0.4% (w/w) curcumin. After incorporation of curcumin, the capsules were dried in a hot air stream to remove traces of acetic acid. The transmission spectra of a plain gelatin capsule and a gelatin capsule coloured with 0.4% (w/w) curcumin, both dissolved in 5 ml water, is shown in Fig. 1. The transmission of light is

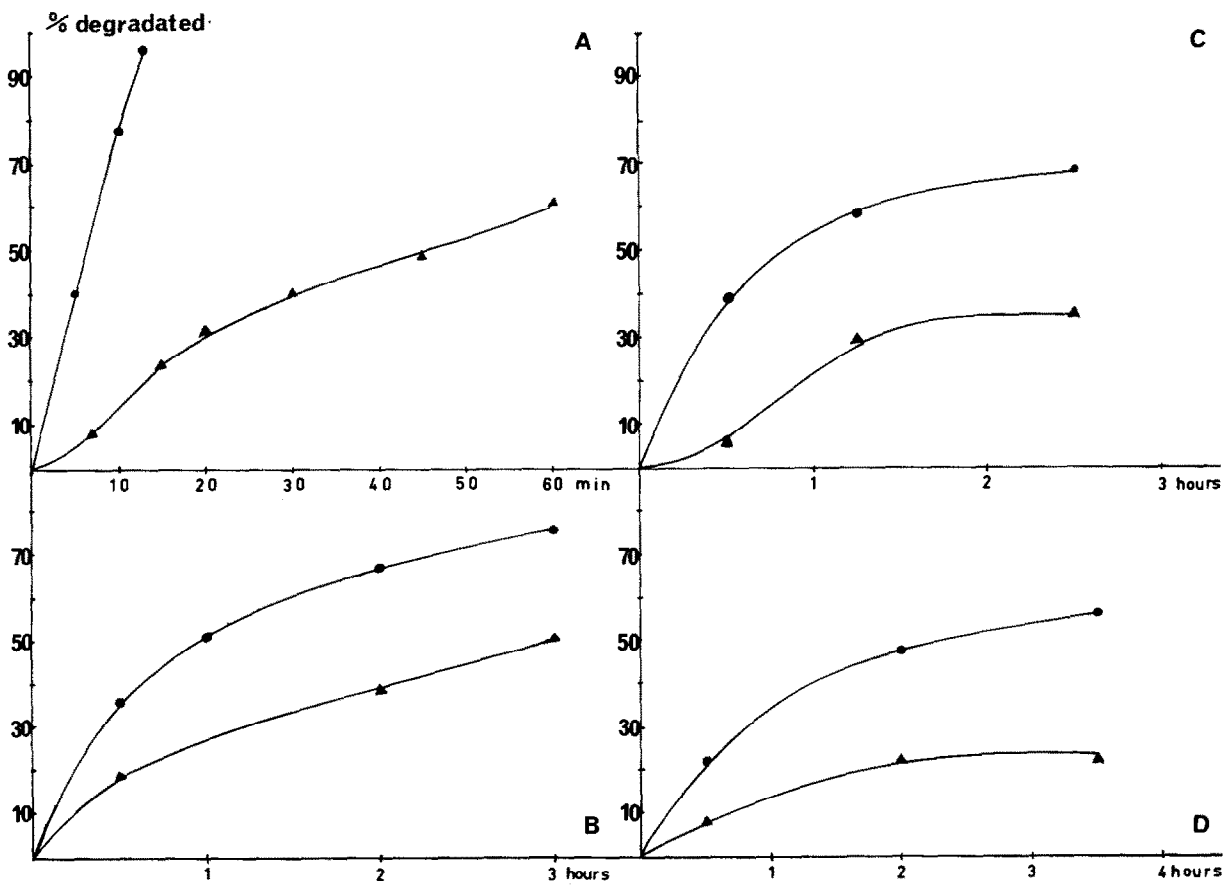

Fig. 2. A: nifedipine. B: chloramphenicol. C: frusemide (urosemide). D: clonazepam. ●, capsule shell without curcumin; ▲, capsule shell coloured with curcumin.

reduced in the wavelength area 300–500 nm (UV-B, UV-A and part of the visible spectrum) in a curcumin-coloured capsule compared to a plain capsule shell. Within these wavelength limits irradiation will cause degradation of several drugs if no protection is offered. It is well known that many commonly used drugs are photolabile (Tønnesen and Karlsen, 1984). Nifedipine (antihypertensive), chloramphenicol (antibiotic), frusemide (furosemide) (diuretic) and clonazepam (antiepileptic) which all show photochemical degradation were chosen as test compounds. The drugs were dissolved in polyethylene glycol 400 (PEG 400) which is a commonly used solvent in combination with soft gelatin capsules. The solutions were filled in plain capsules and in curcumin-coloured capsules. The capsules were irradiated with light of 240–600 nm (Heraeus immersion lamp system). The difference in drug content in coloured and non-coloured capsules after fixed irradiation times was measured by means of HPLC. The results are given in Fig. 2. A curcumin content of 0.4% (w/w) in the capsule shells results in a 3-fold or more increase in the half-life of the test compounds. A curcumin content of 0.02% (w/w) resulted in 20% increase of the half-life for nifedipine. These experiments indicate that curcumin is suitable as a colour stabilizer for soft gelatin capsules containing photolabile drugs and should be considered as an alternative to the synthetic dyes or inorganic pigments frequently used.

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