A021 Inhibition of enzymatic and cellular superoxide anion generation by polygalloylglucose esters.

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The use of tannic acid in the treatment of burns has a long and successful history (1). In the early nineties, preliminary experimental and clinical studies confirmed these positive reports from the past and indicated that highly purified tannic acid (HPTA) might be of interest as a valuable additional therapeutic regimen to improve long-term wound-healing characteristics after thermal injury (2,3). As a first step in the process of elucidating its mechanism of action, we studied the effects of HPTA and its constituting polygalloylglucose esters on superoxide anion (O_{2^-}) generation since this radical, in addition to other reactive oxygen species, is associated with the tissue damage seen in burn patients (4). HPTA was found to be a potent inhibitor of the two major O_{2^-}-generating systems in the burn wound, the enzyme xanthine oxidase and stimulated polymorphonuclear leukocytes. With respect to the inhibition of xanthine oxidase, penta- to nonagalloylglucose showed an activity similar to HPTA, whereas tetragalloylglucose was significantly less active. Towards the cellular O_{2^-} generation, a clear distinction could be made between the effects of polygalloylglucose esters with 4-6 and 7-9 galloyl moieties. The latter compounds were not only significantly more active, but also a difference in the mode of action was observed. Thus, for hepta- to nonagalloylglucose inhibition of the O_{2^-} generation by polymorphonuclear leukocytes appeared to be receptor-mediated. In contrast, the inhibitory effects of tetra- to hexagalloylglucose were entirely related to the radical scavenging activity of these compounds. Monomeric gallic acid was not able to inhibit enzymatic and cellular O_{2^-} generation.

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A022 Effects of the pharmaceutical dosage form on the biological activity and stability of tannic acid

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Tannic acid (TA) has in the past been succesfully used for the treatment of burns, in particular in the period between 1920 and 1940 just before the introduction of penicillin (1). Due to alleged hepatotoxic effects it became obsolete in subsequent years (1). In the early nineties however, TA treatment has again regained interest for its potential beneficial effects on wound healing. It was shown that TA reduced inflammation and positively influenced granulation tissue formation, re-epithelialization, and scar-tissue formation (2,3). Prior to further animal experiments and clinical trials, we studied the influence of the pharmaceutical dosage form on the biological activity and stability of TA. For this purpose, 0.5 and 5.0% (w/w) TA preparations on basis of different ointment and cream formulations were compared with aqueous TA solutions of equal strength. The protein-binding capacity and antioxidant activity were chosen as important determinants to predict the *in vivo* efficacy of these formulations. Protein binding was measured as the ability to cross-link collagen (4). Cross-linking was found to be strongly dependent on the water content of the formulations, being most pronounced in the aqueous reference solutions and hydrogel. Although less distinct, a similar tendency was observed with regard to the antioxidant activity, assessed as the decolorization of the 2,2-diphenyl-1-picrylhydrazyl free radical (5). The stability of the formulations was determined by HPLC analysis of the free gallic acid content (6) after three and six months. In contrast to the results of the biological tests, the stability of TA proved to be significantly better in the apolar ointments.

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