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Effects of dimethyl sulphoxide (DMSO) on aggregation of human blood platelets

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The effects were examined of the universal solvent dimethyl sulphoxide (DMSO) on human platelet aggregatory activity, in-vitro, of the endogenous mediators ADP, adrenaline, arachidonic acid, collagen and PAF-acether which are believed to play important roles in cardiovascular diseases in man. DMSO inhibited aggregation induced by all of the mediators in the order ADP > adrenaline = arachidonic acid = PAF-acether > collagen. Since DMSO is widely used as a solvent for drug substances, an awareness of its intrinsic activity in any such evaluations is essential.

Dimethyl sulphoxide (DMSO) was first synthesized over a century ago (Saytzeff 1867), though its useful solvent properties in relation to a variety of chemical substances have been recognized only within the last fifty years. It has, also, a wide spectrum of pharmacological activity of itself (David 1972; Haigler 1983; Brayton 1986) and has received renewed interest in the last few years as a therapeutic agent, particularly in North America. However, in view of reports linking DMSO to cataracts in laboratory animals (Rubin & Barnett 1967), and debate about its carcinogenic potential, some have cautioned its clinical use until adequate safety data become available (Savastano 1984).

Intravenously administered DMSO has been shown in-vivo to reduce the thrombotic response to surgical trauma (Dujovny et al 1983) in the rat and in a mouse model of pial arteriolar injury (Rosenblum & El-Sabban 1982) and to have anti-thrombotic effects when applied topically to rats (Gorog & Kovacs 1975). However, only few reports have appeared examining the effects of DMSO on platelet aggregation in-vitro, and of these there has been demonstrated an action against effects induced by ADP and adrenaline (Schiffer et al 1976) as well as thrombin (Holz & Davis 1972) and collagen (Shepherd et al 1984).

In view of the growing interest in discovering agents which beneficially modulate the roles of endogenous mediators in thrombosis and cardiovascular disease states, we have undertaken a systematic study of the effects of the universal solvent DMSO on aggregation of human platelets induced by ADP, adrenaline, arachidonic acid, collagen and PAF-acether.

Methods

Our studies of platelet aggregation were performed on citrated platelet-rich plasma (PRP). Blood was obtained via an antecubital vein from fasted healthy male adults who had not received any medication for at least one week before bleeding. PRP was prepared by centrifuging the citrated blood sample (9 volumes of blood to 1 volume of 3·8% aqueous sodium citrate) at 1500 rev min^{-1} for 15 min. The concentration of platelets in plasma was 300 000 ± 50 000 platelets μL^{-1}.

Aggregation experiments were conducted using a Chrono-log aggregometer model 550 (Coultronics), traces being recorded on an Omniscribe recorder. Aggregation was provoked by the following substances at the pre-determined concentrations indicated in parentheses: ADP (4 μM), adrenaline (1 μM), arachidonic acid (0·5 mM), collagen (10 μg mL^{-1}) and PAF-acether (1 μM). All the aggregating agents except PAF-acether, which were purchased from Sigma, were dissolved in physiological saline. PAF-acether (obtained from Bachem Corporation) was dissolved in 2·5% w/v aqueous bovine serum albumin (Fraction V).

Aggregation studies were conducted essentially as

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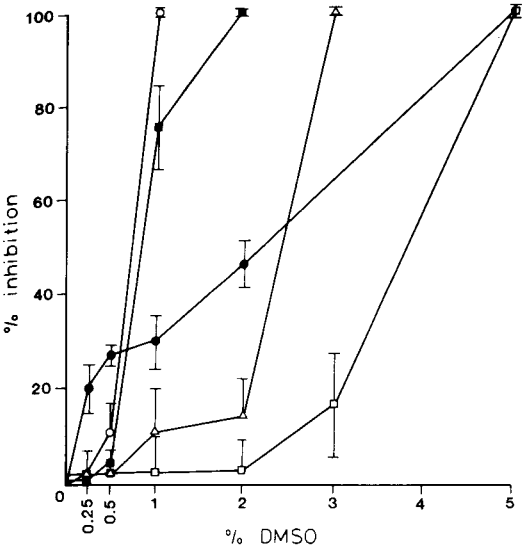

FIG. 1. Dose-response curves demonstrating the effect of dimethylsulphoxide (DMSO) on aggregation in human platelets induced by previously determined concentrations of ADP (●——●), adrenaline (○——○), arachidonic acid (△——△), collagen (□——□), and PAF-acether (■——■). Each curve is the mean ± s.e.m. from four experiments.

described by Born & Cross (1963). Estimates were made from the recordings of optical density changes and the percentage of inhibition of platelet aggregation (induced by each of the agents mentioned above) by the presence of each of the following concentrations of DMSO calculated: 0·25, 0·5, 1, 2, 3 and 5%. Four aggregations on different PRP were undertaken for each DMSO concentration.

Results and discussion

The results are indicated in Fig. 1. In essence, DMSO produced a significant inhibition of platelet aggregation provoked by all of the agents examined, being most potent (at a starting concentration of 0·25%) against aggregation induced by ADP, intermediately and equipotent (0·5% DMSO) against aggregation due to adrenaline, arachidonic acid and PAF-acether, and least potent (DMSO concentration 2%) in the case of collagen-induced aggregation.

The aggregating agents used in these studies are believed to play a role in cardiovascular disease in man. It is evident therefore that an awareness of these observed effects of the universal solvent DMSO is extremely important in the evaluation of any potential chemotherapeutic agent where DMSO may be the vehicle.

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