DMSO REPRESSES INFLAMMATORY CYTOKINE PRODUCTION FROM HUMAN BLOOD CELLS AND REDUCES AUTOIMMUNE ARTHRITIS

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Dimethyl sulfoxide (DMSO) is currently being used by many people, both topically and orally, to treat inflammatory conditions as well as cancer. However, little is known about the efficacy, safety and mechanism of action of DMSO in humans. We therefore examined the effects of this polar solvent on whole human blood, stimulated or not, *ex vivo*, with E. coli. We found that, between 1 and 2%, DMSO markedly inhibited cytokine production without affecting cell viability. However, at greater than 5%, significant death of leukocytes was observed, suggesting that DMSO has only a narrow window of efficacy. The two *in vivo* generated metabolites of DMSO, dimethyl sulfide (DMS) and dimethylsulfone (DMSO2), required higher concentrations than DMSO to be anti-inflammatory. Mechanism of action studies using purified human monocytes revealed that DMSO's anti-inflammatory properties were due, at least in part, to inhibition of the ERK1/2, p38, PI3K and JNK pathways. *In vivo* mouse model studies revealed that topical administration of DMSO did not reduce the growth rate of subcutaneously implanted B16 melanoma cells, even though it did act in vitro to increase their differentiation. Importantly, however, topical administration of DMSO significantly ameliorated KBxN-induced arthritis in mice and this was associated with lower levels of inflammatory cytokines in the joints. Taken together, our studies suggest that DMSO may be useful for some inflammatory conditions but care must be taken to avoid toxic effects.