Letter to the Editor

DRUG COMBINATIONS

Sir,

I would prefer to employ the more appropriate term in your editorial comment rather than the word 'Polypharmacy' used by Dr. Madan in his guest editorial (Ind. J. Physiol. Pharmac., July 1971). Despite the rapid advances in the field of Pharmacology, better understanding of the mechanism of drug action and an increasing awareness of drug interaction, the drug combinations continue to enjoy great popularity amongst the physicians - a fact that cannot be easily ignored. Instead of heaping more condemnation on this oft-condemned commodity, it will serve more useful purpose to go into the origin *i.e.* the very raison-de-etre of the drug combinations and to analyse the factors responsible for their patronage. Constructive criticism coupled with sympathetic understanding can result in suggestions to bring some order to therapeutic jungle and to provide pointers regarding what can easily be accepted and what must be rejected.

It is not sufficient to accept the limitations of all drugs in terms of safety and efficacy but we must also realise the paucity of diagnostic facilities available to practitioners to understand the prevailing situation. A practitioner even in Western countries, leave alone in a town or village in India, is very often called upon to prescribe for a patient whose illness he has yet to diagnose either because of the complexity of the disease or due to the high cost involved or non-availbility of laboratory investigations. It is no doubt better to treat the patient with a single drug in effective doses. Unfortunately, there are very few conditions where such an approach is possible. Either, the patient has more than one illness or the diagnosis is not certain, or none of the available drugs is suitable to be used alone on grounds of safety, efficacy, convenience, etc.

Dr. Madan's comment "fixed dose combination of a newly discovered antimicrobial agent with dobious efficacy, narrow spectrum of activity and undesirable properties arise because of commercial interest" is difficult to understand or substantiate and perhaps based on a lack of understanding of the process of drug development in India or abroad. In India, at least, any new drug is investigated as a single drug and then if need be, in combination with some other drug after extensive animal studies and only with *prior* permission of Drugs Control authorities. 'Marketing' permission could be expected if the result of the clinical studies show that the combination has some advantage in terms of safety or efficacy over its constitutents in the opinion of the Drugs Control authorities as well as the 'experts'. Your readers will be interested to know that any 'new' (single or combination) drug marketed in the last few years in India has also been approved by the 'experts' who are usually professors of pharmacology, medicine or other related faculties or by bodies like Indian Council of Medical Research.

One could agree with Dr. Madan that there are some odd mixtures that cannot be justi fied on any grounds and no inconvenience to the patient or the doctor would result if thes are eased out. Your readers must surely be aware of the efforts being made by the Drug Controller, India, to collect the medical opinion on the safety and efficacy of a number o fixed ration combin ations. It has, of course, followed the American FDA's action on th basis of the NAS-NRC reviews.

Why do drug manufacturers in India, on occasions, will study and try to market combi nations? The principal reasons are the same as those applicable outside India, namely, fo synergistic effect, to reduce side-effects, to prevent resistance, to extend antimicrobial coverag for convenienee and also in many cases, to lower the cost. As is metioned above, unless som of these reasons are substantiated, it is unlikely that any reputed 'foreign' or Indian firm woul get the necessary permission from New Delhi.

The marketing managers of drug companies would be very happy if "the colourfu brochures and pamphlets which sing the siren song of the purveyor of pills, dominate th thoughts and beliefs of the prescriber" was indeed the case. Perhaps Dr. Madan places too much faith in the influence of advertisements and little in the discriminating knowledge o the medical practitioners which include the teaching staff of over 100 medical colleges and a large number of specialists. Doctors are human and to some extent may be affected by advertising but usage of drugs that is not backed by therapeutic efficacy tends to be short lived as has been easily borne out by the history of therapeutics.

The examples of adverse reactions cited by Dr. Madan should draw our attention to the indiscriminate use of drugs in general rather than the combinations. It is not the drug but its usage that is at fault in these cases. Such mishaps can be prevented if the use of drug combinations is restricted to well studied and approved clinical indications.

All physicians are expected to make an effort first to use only a single effective drug and only in clearly defined selected conditions. In ill defined situations two drugs and that too occasionally in fixed-ratio combinations, are to be employed. It goes without saying that there should be some of the above mentioned justifications for the use of fixed-ratio combi nations. Hence, the solution to the problem lies in teaching and practising rational thera peutics, bettering the facilities for diagnosis and bringing up-to-date the specifications and recommendations for the use of drug combinations after a careful look at the available drugs.

Lastly, let us not forget that not all 'experts', even those who chaired the NAS-NRC panels, were certain that all their recommendations were based on unequivocal evidence (L. Lasagna; One man's odd is another man's even; Clin. Pharmacol. Ther.; 11 : 443, 1970). It would, therefore, be a pity if because of some poor combinations, many others which con tinue making a contribution to practical therapeutics are lost.

DILIP J. MEHTA, M.D., PH. D.
Hoechst Pharmaceuticals Ltd.
Bombay