

C7-128
PN-ABM-717
7986E

FINAL REPORT

Covering Period: 24 Aug. 1987 - 31 Dec. 1990

**Submitted to the Office of the Science Advisor
U.S. Agency for International Development**

PROTEIN BINDING OF DRUGS IN MALNUTRITION AND PARASITIC DISEASES

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Project Number: C7-128

Grant Number: DPE-5544-G-SS-7056-00

A.I.D. Grant Project Officer: Ms. Joyce Frame

Project Duration: 24 Aug. 1987 - 31 Dec. 1990

Rec'd in SCI AUG 13 1991

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EXECUTIVE SUMMARY

The purpose of this project has been to investigate and describe the influence of two conditions that are prevalent in developing countries, namely malnutrition and parasitic disease, on plasma protein profiles and protein binding of medicines. The latter is an important determinant of the action and fate of medicines in the body. The results presented in this report show that both plasma protein profiles and the way they bind medicines change significantly in parasitized hosts and in the malnourished. These changes have not been recognized previously and could provide the basis for new dosage recommendations for large populations in the developing world.

The collaborating scientists in Nigeria and their colleagues, as well as the international scientific community, through publication of this paper, will now be aware of specific peculiarities of large patient populations in developing countries in their response to medicines. Also, the collaborating scientists are now in the position to pursue similar phenomena as they relate to other medicines and to other patient populations in their country. The skills and methodology have been acquired, although they may be restricted by availability of instrumentation or the lack of it. This difficulty can be overcome by careful selection of test medicines that can be analyzed by available means.

RESEARCH OBJECTIVES, METHODS AND RESULTS

These are discussed in the enclosed manuscript, submitted for publication to the European Journal of Clinical Pharmacology.

IMPACT, RELEVANCE AND TECHNOLOGY TRANSFER

The findings of this project do not have immediate direct implications on everyday patient care. Nevertheless, these data will undoubtedly increase awareness and knowledge among scientists and physicians, both in developing countries and worldwide, of specific pharmacokinetic problems in large groups of patients in the developing world. The present investigation should be followed by direct investigation of the pharmacokinetic behavior of drugs in these groups of patients. One may predict that the alterations that were observed in key plasma protein levels and subsequently in the protein binding of drugs will translate into real modifications of pharmacokinetic parameters in patients. The immediate conclusion from such studies could then be translated into altered dosage recommendations for malnourished or parasitized patients, i.e., improved patient care.

The collaborating scientist, Dr. Emudianughe, spent a year training in Beer-Sheva. During this time he acquired expertise in both general and specific methodology that was used in the present project. This expertise will hopefully be used in the future scientific career of Dr. Emudianughe. Also, being responsible for the teaching of clinical pharmacology in the Ilorin School of Medicine, the new awareness that was acquired will be transferred to medical students in that campus.

PROJECT PRODUCTIVITY

The general goals of the project were accomplished in that target plasma protein profiles and binding of the model drugs were investigated and revealed the differences that had been anticipated. A secondary goal, namely the development of an equilibrium electrophoresis method for the study of binding to individual plasma proteins could not be accomplished. Multiple trials were made under a variety of buffer, pH, matrix and voltage conditions. None proved adequate for the purpose. It must be noted that the feasibility of development of such a method was questioned since the outset, but was still considered worthwhile trying.

FUTURE WORK

As discussed above, clinical trials on the pharmacokinetics of model drugs in malnourished and parasitized patients should be initiated.

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