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Research of New Drugs for Idatitis (**) 

I will not get involved in the definition or the interpretation of "Orphan Drugs" since this aspect of the problem has been debated, both here and in the past, by much more qualified people. I will limit myself to the illustration of a small research program we have set up to give our contribution to a problem which can be considered as belonging to the subject (or an aspect) of this meeting.

In planning new research areas for the Laboratory of Medicinal Chemistry of the Istituto Superiore di Sanità, following the suggestion given by Professor G. Segre about the opportunity to consider the area of orphan drugs, we chose echinococcosis-idatitosis as our field of intervention. Such a choice was made based on three main considerations: i) the WHO recommendations on the topics of international interest; ii) the incidence of such a disease in depressed areas of Italy and the consequent not irrelevant impact on the national economy; iii) the existence in our Institute of the scientific "competences" necessary to starting up a research program, at least for its first stages. The plan I will briefly illustrate now is the result of the combined efforts of the Departments of Pharmacology (Prof. V. Longo), Parasitology (Prof. A. Mantovani), Medicinal Chemistry (Prof. G. Settimi) and Veterinary Medicine (Dr. R. Lorenzini) of our Institute. The overall strategy for a start involved three main steps: i) a suitable biological model; ii) the study of the action on such a model of well established drugs for controlling the disease; iii) the testing in such a model, of new potential drug candidates, of synthetic as well as of natural origin.

The biological test consists of a first stage of in vitro assays: the protoscolyces of Echinococcus granulosus will be exposed to suitable concentrations of the compound to be tested and their ability to develop the evagination stage evaluated according to the test elaborated by Wikerhauser.

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The well established drugs to be considered as experimental guidelines for the evaluation of their action(s) on the biological model are: Mebendazole, Flubendazole, Albendazole, Griseofulvin, Dapsone, Quinol, Vinblastine.

The action of the above-reported drugs will be monitored both by examination of the histological and biochemical modifications induced in the model. Also from the chemical standpoint, analytical methods will be assessed in order to follow up their concentration outside and inside the tissue under examination.

The new synthetic products to be tested will consist of the molecules so far reported to be active, but conjugated to "carriers" in order to cross the cellular barrier, and of new compounds inspired to the structure of the natural compound to be screened in the chosen biological model, should they prove to be active.

The natural compounds which will be subject to our screening will be chosen among those isolated by us in the past which resulted highly cytotoxic from our researches on biologically active compounds, and will include Quassin, Flavipucine, Atlantadone, Grosheimine and the Leucinostatines.

It is not our aim, nor our hope, to find a new effective drug for eradicating the disease: we will consider ourselves sufficiently rewarded if we succeed in giving a positive contribution to the understanding of some aspects of the mechanism of action of drugs against an orphan disease and to the scientific improvement of developing countries.