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COMMITTEE ON RESEARCH  
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COUNCIL ON PHARMACY AND CHEMISTRY  
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American Medical Association

Grant No. \_\_\_\_\_

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SUBCOMMITTEE ON  
GRANT-IN-AID

APPLICATION FOR GRANT-IN-AID  
(Please Submit Six Copies)

Date: January 26, 1956Name of Applicant: William G. Figueroa, M.D.Title: Assistant Professor of MedicineInstitution: University of California at Los Angeles, School of MedicineAddress: Los Angeles 24, CaliforniaTitle of Project: Evaluation of Chelating Agents as Therapeutic Agents  
in Acute Intestinal Iron Intoxication.Sum Requested: \$500.00 Purpose for which funds are to be used: Purchase of:  
Radioactive iron, dog food, chemicals and glassware.

Brief Description of purpose of research and methods to be employed:

In the past few years an increasing number of fatal poisonings in children following the ingestion of ferrous sulfate tablets have been reported. (1-16) The intravenous administration of certain iron preparations may also result in manifestations of mild to severe toxicity.

In combating the shock that often develops, the only recourse so far has been the use of fluids and stimulants. If a drug could be found that combines with the excess iron circulating in the blood and increases the excretion of iron from the body, it would seem that one might be able to counteract some of the toxic effects of the iron. There are a few cases on record in which a concentration of iron in the serum of both man and animals suffering from acute iron poisoning was from 15-100 times the normal. Under these circumstances, it is to be presumed that the iron circulating in the plasma is "unbound" and may act as the toxic agent. In a previous report, we have shown that the use of a chelating agent such as calcium disodium (EDTA) effectively binds iron in the blood and, (Extra sheets may be used to expand this description. Please give pertinent references, if any, to published papers from your laboratory on this subject.)

Expected Duration of Study: Two YearsSources of other funds used to support this project: 1) Riker Laboratory, Los Angeles, California. 2) Research funds from the Veterans Administration.Facilities available: Research Laboratories of the Isotope Unit, Metabolic Unit, Hematology Unit, Veterans Administration CenterHas this work previously been supported by A.M.A. funds? NO

Signature of authorized officer of institution: \_\_\_\_\_

Robert Gordon Sproul

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Brief description of purpose of research and methods to be employed:

(Cont.)

in certain diseases where iron is stored in excess, increases its excretion as much as 10 to 15 fold in the urine. (17)

By employing the method of Reissmann (18, 19) in a limited number of dogs in which we induced acute iron poisoning by introduction of a solution of ferrous sulfate into the intestine and administering Ca EDTA intravenously, excretion of Fe in the urine increased by a factor of 20-40 times the control levels. These preliminary observations may indicate that the "unbound" fraction of excess iron in circulation was chelated and excreted in the urine.

Since our experience indicates that the disodium calcium salt of ethylenediaminetetraacetic acid is of low toxicity for man, and since initial observations in acute experimental iron poisoning in dogs have been encouraging, it seems pertinent to continue the investigation of the protective action of calcium EDTA and other similar agents with a greater affinity for iron. It is proposed to administer toxic doses of iron salts to dogs whose reaction and survival will be observed, both with and without treatment with chelating agents. In these experiments analyses will be made of the iron content of serum, urine and feces employing standard chemical methods and also using the isotope technique by incorporating  $Fe^{59}$  as a tracer in the salts administered. Should an opportunity arise to observe acute iron poisoning in man, the protective action of chelating compounds will be tried and similar analyses performed.

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