HEMOSORPTION

Y. M. LOPUKHIN M. N. MOLODENKOV

HEMOSORPTION

Y. M. LOPUKHIN, M.D.
Academician, USSR Academy of Medical Sciences,
and Rector, Second Moscow Pirogov Medical Institute,
Moscow, USSR

M. N. MOLODENKOV, M.D.
Professor, Second Moscow Pirogov Medical Institute,
Moscow, USSR

Translated from Russian by

Nicholas Bobrov and **Ludmila Aksenova**
Moscow, USSR

Illustrated

The C. V. Mosby Company
ST. LOUIS • TORONTO • LONDON 1979

Published as *Gemosorptsiia* © 1978 by
Meditsina Publishing House, USSR

Printed in the United States of America

The C. V. Mosby Company
11830 Westline Industrial Drive
St. Louis, Missouri 63141

Library of Congress Cataloging in Publication Data

Lopukhin, IUriĭ Mikhaĭlovich.
Hemosorption.

Translation of Gemosorptsiia.
Bibliography: p.
Includes index.
1. Artificial liver. I. Molodenkov, Mikhail Nikolaevich, joint author. II. Title.
RC846.L6613 617'.556 79-1273
ISBN 0-8016-3029-0

CB/CB/B 9 8 7 6 5 4 3 2 1 01/D/038

FOREWORD

This English edition of a book by Russian authors exists because of two fortunate circumstances: the great experience gained, both experimentally and clinically, in hemosorption by our fellow workers and colleagues in the Soviet Union, which in our opinion is of certain scientific interest, and, what is of greater importance, The C. V. Mosby Company's worthy appraisal of the world-wide significance of international scientific contacts, which promote mutual understanding and détente in our unstable world.

In the Soviet Union, this book was published in Russian by Meditsina in 1978.

In this work, all the quantitative indices are given in SI units, and this may be unusual for the reader at large.

Y. M. Lopukhin
M. N. Molodenkov

PREFACE

At the end of the 1960's, our collective began working on a device that could compensate for the detoxifying function of the liver. Experiments that were being actively carried out in liver transplantation (Lopukhin et al., 1971) obliged us to deal with this problem. The future "artificial liver" was to perform at least two functions: prepare a seriously ill patient with a liver affection for an operation and help him recover after transplantation if the transplanted liver temporarily failed to function.

At the time, kidney transplantation was in a similar situation, as was well known to one of us (Lopukhin et al., 1969). The achievements in clinical kidney transplantation were largely due to perfect hemodialysis—i.e., to the artificial kidney. We knew quite well that our task, which was far greater than liver transplantation proper, could be satisfactorily tackled only if different specialists, such as mathematicians, chemists, physicists, biochemists, engineers, physiologists, experimenters, and surgeons, pooled their efforts.

This book in essence sums up the initial results of the activity jointly carried on by different scientific institutes and medical establishments which have a common aim and which are under the aegis of the State Committee of the USSR Council of Ministers for Science and Technology.

The key chemical problems were solved in the Mendeleyev Moscow Chemical and Technological Institute, the Mineral Fuel Institute, the Physical Chemistry Institute, the Vernadsky Institute of Geochemistry and Analytical Chemistry, the Gubkin Moscow Institute of the Petrochemical and Gas Industries, and the Ministry of the Chemical Industry.

The engineering and physical problems were worked out in the All-Union Scientific Research Institute of Medical Technology, the All-Union Institute of Current Sources, and the Leningrad University.

This work was actively carried on also by the personnel of the Institute of Medico-Biological Problems, the Institute of Organ and Tissue Transplantation, and the All-Union Scientific Research Institute of Disinfection and Sterilization.

Experimental and clinical investigations were carried out mainly at the Scientific Research Center and the clinics of the Second Moscow Pirogov Medical Institute.

Many investigations were carried out in the Sklifasovsky All-Union Scien-

tific Research Institute of Emergency Medical Aid, the Moscow Dental Institute, and the Altai Medical Institute.

A new method of detoxifying and correcting humoral hemostasis, which we termed hemosorption (Lopukhin et al., 1971), had been worked out, perfected, and tested as a result of the activity jointly carried on by the aforementioned institutions.

Clinical investigations, which in essence are only the start, give us every reason to assert that hemosorption is the most effective therapeutic method in several pathologies (exogenous poisoning and all types of hemolysis). In other cases (hepatic failure, hepatoses, pancreatitis, hyperkalemia, hyperammonemia, etc.), it is very useful for complex therapy. Moreover, it is promising and deserves great attention as regards several illnesses, especially those that cannot be cured at present (hypercholesterolemia in the case of atherosclerosis, late toxemia of pregnancy, and cerebral coma).

It was over fifty years ago that the first primitive colloid tube was immersed in a salt solution in a vessel to imitate kidney function (Abel et al., 1913).

In our age, when science and technology are rapidly developing, the inherent disadvantages of hemosorption probably will soon be overcome and the method put to good use on a wide scale for the noble cause of curing the ill, saving lives, and protecting health.

It is our hope that this book will stimulate doctors and scientists to become interested in hemosorption, thus promoting its further development.

Y. M. Lopukhin
M. N. Molodenkov

CONTENTS

1 Introduction, 1

Historical background, 1
Hemosorption and the liver, 4
Two unsolved problems of sorbent chemistry, 8
Fields of application of hemosorption, 9

2 Sorbents, 11

Activated carbons, 12
  Method of preparing activated carbons for hemosorption, 24
  Sterilization of carbon sorbents, 25
Ion-exchange sorbents, 26
  Method of preparing and sterilizing ion exchangers for hemosorption, 34
Investigation of the toxicity of sorbents, 34

3 Mathematical analysis of hemosorption, 36

Mathematical analysis of hemosorption on carbon sorbents, 36
  Calculation of the processes of competitive sorption in multicomponent mixtures, 36
  Quantitative analysis of carbon sorbent properties, 38
Mathematical analysis of hemosorption on ion-exchange resins, 48

4 Hemosorption apparatus/Hemosorption methods, 57

Methods of giving hemosorption treatment to adults, 59
Preparation of the apparatus for hemosorption, 60
Hemosorption methods, 61
  Hemosorption by means of the extracorporeal circulation machine—antigravitation flow, 63
  Hemosorption by means of the extracorporeal circulation machine—gravitation flow, 64
  Hemosorption without the extracorporeal circulation machine, 65
  To-and-fro hemosorption, 65
  Hemosorption under static conditions, 68
Methods of giving hemosorption treatment to children, 69
Hemosorption apparatus of the system worked out by the All-Union Scientific Research Institute of Medical Technology, 70
Hemosorption apparatus designed by the Sklifasovsky All-Union Scientific Research Institute of Emergency Medical Aid, 72

5 Premedication/Anesthetization/Control and correction of hemodynamics in hemosorption, 75

Premedication, 75
Anesthetization, 76

Hemodynamics when hemosorption treatment is given to adults, 77
Hemodynamics when hemosorption treatment is given to children, 88
Acid-alkali state of patients during hemosorption treatment, 90

6 Coagulating system and morphologic blood elements in hemosorption, 93

Coagulating system, 94
Experiments, 94
Clinical studies, 100
Blood cells, 105
Experiments, 105
Clinical studies, 108

7 Lymphosorption, 112

Methods of stimulating lymph drainage, 114
Lymphosorption, 116
Experiments, 116
Clinical studies, 116

8 Plasmasorption and plasmapheresis, 122

Methods of plasmapheresis with plasma exchange and plasmasorption, 122

9 Immunoadsorption, 132

10 Hemosorption in acute poisoning, 141

Poisoning by barbiturates and tranquilizers, 143
Experiments, 144
Clinical studies, 151
Poisoning with organophosphorous insecticides, 168
Poisoning with chlorinated carbohydrates, 172

11 Hemosorption in acute and chronic diseases of the liver, 177

Experiments, 179
Clinical studies, 189
Clinical characteristics of patients with hepatic failure, 189
Hemosorption in cholelithiasis and tumors of the pancreaticoduodenal region, 195
Hemosorption in cirrhosis of the liver, 204
Hemosorption in hepatic coma, 216

12 Hemosorption in hemolytic states, 224

Experiments, 225
Clinical studies, 230

13 Correction of blood electrolytes by the hemosorption method, 232

Hemosorption in hyperkalemia, 232
Experiments, 233
Clinical studies, 243
Hemosorption in hyperammonemia, 248
System for automatic correction of blood electrolyte composition, 254

14 **Complications in hemosorption,** 258

Collapse-like reactions, 258
Chills, 268
Fibrinolysis, 272
Recurrent coma (recoma), 273

15 **Prospects for the development of hemosorption,** 275

Bibliography, 285

1 Introduction

Historical background

In the literature published outside the Soviet Union, extracorporeal perfusion of blood through columns containing activated carbon or ion-exchange resins for the purpose of eliminating toxic metabolites of an endogenous or exogenous nature from the blood usually is termed hemoperfusion or simply perfusion. Since the mechanism of blood depuration in hemoperfusion is based on sorptive processes (adsorption and absorption), this type of detoxifying therapy in the Soviet Union is called hemosorption (from Greek *haima*, "blood," and Latin *sorbere*, "to absorb" or "to imbibe") (Lopukhin et al., 1972). This term is analogous to the widely accepted term "hemodialysis," and we believe that it quite accurately reflects the essence of the sorptive purification of blood.

The removal of toxins from other fluids of the organism (i.e., lymph, plasma, and liquor) by the adsorption technique was termed lymphosorption, plasmasorption, and liquorosorption, respectively (Lopukhin et al., 1975; 1977).

Apparently, the first to experimentally perfuse blood through adsorbents were Muirhead and Reid in 1948. They reduced the level of uric acid by passing the blood of dogs with experimental acute renal failure through an ion-exchange resin. In 1955, their experiments were repeated by Bronnimann and Pini. The first report on the clinical application of hemosorption was made in 1958 by Schechter et al., who perfused the blood of a comatose patient suffering from hepatocirrhosis through an ion-exchange resin. They thus succeeded in reducing the level of ammonia in the blood, but columns had to be changed every fifteen to twenty minutes because of their rapid "thrombosis." Interest in the sorptive methods of blood depuration was not evident again until 1964, when Bock and Yatzidis, apparently working simultaneously, published reports on the use of activated carbon as an adsorbent.

In his experiments on animals, Yatzidis (1964) proved that activated carbon absorbs creatinine, uric acid, indican, phenols, guanidine bases, and organic acids from the blood. This gave him good reason for using an "effective and simple artificial kidney" to medically treat patients with renal failure.

Patients with uremia underwent hemosorption treatment twenty times, in the course of which the fibrinogen level dropped and the number of thrombocytes in the blood diminished. According to Yatzidis, this occurred because toxic sulfur compounds were washed away from carbon.

In 1965, Dunea and Kolff gave activated carbon hemoperfusion treatment eighteen times to three patients with uremia. A high urea and uric acid clearance was observed only at the initial stage of hemoperfusion; carbon particles in the column were sintered, and the number of thrombocytes in the blood dropped sharply. Patients often had attacks of nausea and vomiting.

In 1966, Hagstam et al. detected carbon particles ranging from 3 mμ to 35 mμ in blood that flowed out of a column containing activated carbon. When a microscope was used for investigation, carbon particles were found in the lungs of all the animals examined, in the spleen of almost all of them, in the kidneys of a smaller number of them, and in cerebral tissues in individual cases.

Similar data were obtained by Barakat and MacPhee (1970). Dutton et al. (1969) showed, in a special investigation of the effect of hemoperfusion on the number of thrombocytes in the blood of cats, that blood perfusion through carbon sorbents with granules of 1.3-1.4 mm at a blood flow rate of 16 ml/min causes a diminution in the number of thrombocytes in an animal's blood by 78% within an hour. Since urea and creatinine are rather poorly sorbed by activated carbons and hemoperfusion is always followed by thrombocytopenia, generalized embolism of the parenchymatous organs by carbon particles, and the sintering of carbon granules in the columns, doubt was cast on the applicability of hemosorption as a substitute for hemodialysis in the treatment of patients with acute and chronic renal failure (Merrill, 1971). Investigations by Chang et al. involving the encapsulation of carbon particles in semipermeable natural and artificial membranes that are compatible with blood (1964-1966; 1968-1970; 1972; 1974; 1975) greatly helped to work out the hemosorption problem further. The granules of the encapsulated adsorbent injure the morphologic blood elements considerably less and make embolism by carbon particles less likely to occur (Chang, 1966; Rosenbaum et al., 1968; Andrade et al., 1972; Vale et al., 1975). Andrade (1972) showed that the number of carbon fragments depends on how well an adsorbent is washed and on its code name. But minute particles are washed away from carbon even when a film having a thickness of 500 $\mu\mu$ is deposited on carbon granules, because polymeric films do not cover all the sharp edges and projections of the granules. Many authors believe that the likelihood of embolism by carbon microparticles is exaggerated (see discussion following article by Andrade, 1972).

As Andrade proved in 1974, blood which perfuses through carbon adsorbents that are washed well contains less carbon dust (0.2 mg per hemosorption treatment) and more silicone rubber particles, which are formed when a roller pump is used in hemosorption. Microcapsulated carbon adsorbents were successfully used by Chang et al. (1970-1972) when patients with uremia underwent hemoperfusion treatment.

The first attempts to use hemosorption in treating patients with hepatic failure were apparently made by the hemosorption laboratory of the Second Moscow Pirogov Medical Institute (Lopukhin et al., 1971).

In 1971, Barakat and MacPhee reported that bilirubin and alkaline phosphatase can be sorbed by activated carbons from bile and urine and from the blood of animals having experimental jaundice caused by the ligation of the common bile duct.

In 1972, Chang made a report on hemosorption effected by means of microcapsulated activated carbons in a patient suffering from alcoholic hepatocirrhosis who was in a hepatic coma with Grade IV encephalopathy. During hemoperfusion through a column containing 200 g of activated carbon for sixty minutes, the patient regained consciousness and the electroencephalogram normalized. But the patient fell into a coma again an hour after hemosorption was completed. The levels of bilirubin, urea, and ammonium in the patient's blood prior to and after hemoperfusion remained the same. Chang believes that the patient regained consciousness during hemosorption because carbon adsorbed toxic metabolites of a protein nature.

Gazzard et al. (1974) successfully employed hemosorption on activated carbon to bring twelve of twenty-two patients out of a deep hepatic coma caused by massive hepatic necrosis as a result of viral hepatitis and hepatotropic poisoning. Patients in a coma well endured hemoperfusion through a column containing 200 g of microcapsulated activated carbon for four to eight hours daily. The perfusion rate was 300 ml/min. Patients began to regain consciousness twenty to twenty-five hours after the initial hemosorption treatments. Gazzard and fellow workers attribute the hemoperfusion effect to the adsorption of cerebrotoxic amino acids (phenylalanine and others) by carbon granules. Although the carbon coating was compatible with blood, up to 70% of the thrombocytes were destroyed during every hemosorption treatment; according to the investigators, this caused the cerebral hemorrhage and death of three patients. The puncture biopsy of the liver, which was made six months after the patients were discharged from the clinic, showed that the cytoarchitectonics of the liver was normalized.

Willson et al. (1972; 1974) published data on the sorption of cholephilic anions by the resins Amberlite XAD-2 and Dowex-1. A 1,000 cc column containing 500 g of the resin Amberlite XAD-2 extracts 45-50 mg of bilirubin in two hours of perfusion at a blood flow rate of 50 ml/min, whereas the resin Dowex-1 extracts 50-60 mg under the same conditions.

Weston et al. (1974) carried out experiments on dogs to determine whether bilirubin was capable of undergoing selective adsorption with the aid of the neutral ion-exchange resin Amberlite XAD-2. Several hours after the portacaval shunt and the ligation of the hepatic artery, dogs began to show symptoms of hepatic ischemia and hepatic coma. Their blood was perfused through a column containing 400 g of the resin for six hours.

The duration of hemosorption was limited due to the development of the

hemorrhagic syndrome caused by the massive destruction of thrombocytes on the sorbent surface. The rate at which blood flowed through the column was maintained by means of a roller pump. Prior to perfusion, the resin was washed with a physiologic salt solution containing heparin. In the course of perfusion, 200 units of heparin were introduced into the arteriovenous shunt every hour. Pressure fell sharply during hemoperfusion, and there was pronounced intraperitoneal hemorrhage in four dogs. In these animals, the level of thrombocytes in the blood constituted only 20% of the initial level after eight hours of perfusion. In an hour of perfusion, 75-90% of the leukocytes circulating in the organism were destroyed. The concentration of amino acids, ammonium, lactate, and pyruvate did not change when blood was perfused through the resin. The animals did not live longer than those of the control group. Bilirubin was sorbed during perfusion.

Yatzidis (1965) was apparently the first to use hemoperfusion for treating exogenous poisoning. He employed activated carbon for adsorbing barbiturates from the patients' blood. Later, it was proved that hemosorption was effective in treating poisoning caused by soporifics, neuroleptics, organophosphorous compounds, hepatotropic poisons, meprobamate, digitalis, phenacetin, atropine, and morphine (Hagstam et al., 1966; De Myttenaere, 1967; Bakhin and Mashkov, 1972; Chang, 1973, 1974; Burkov et al., 1974; Winchester et al., 1974; Barbour et al., 1975; Komarov et al., 1975; Lopukhin et al., 1975, 1976, 1977; Vale et al., 1975; Castro and Kessel, 1976; Goulding, 1976; Leber, 1976; Lushnikov et al., 1977). In the Soviet Union, all hemosorption researches have been carried out in the Second Moscow Pirogov Medical Institute since 1970.

Hemosorption and the liver

There is every reason to believe that the detoxifying function of the liver is its most essential and vital function. The organism rapidly and inevitably dies when this function ceases, as is borne out by convincing experimental material (Eck, 1877; Pavlov, 1892). The detoxifying function of the liver is not only vital, but also indispensable, because no other system in the organism can compensate for its loss. This function can be reproduced artificially in several ways: (1) by the use of live dissociated allogeneic and xenogeneic hepatic cells, (2) by the use of "artificial cells" (Chang, 1972) as microcapsules containing enzymes that ensure the synthesis of urea, the formation of paired sulfoethereal compounds, glucuronides, etc., (3) by the creation of an artificial detoxifying-excretory system, and (4) by the use of sorbents to bring about the sorption of xenobiotics and endogenous toxins directly from the blood.

(1) *Detoxifying function of the liver reproduced artificially by the use of live dissociated allogeneic and xenogeneic hepatic cells.* Such cells can partially compensate for the detoxifying function of the liver when they are introduced intravenously, subcutaneously, or intraperitoneally as suspensions in a dose of at least 10^5-10^6 cells (Ostroverkhov et al., 1975). Archakov (1974) suggests that

the microsomal fraction of the hepatic cells can be used instead of the whole cells for this purpose, because the enzymatic systems that make the detoxifying function possible are localized mainly in the endoplasmic reticulum. This method is still confined to experiments due to the functional inconstancy of the dissociated hepatic cells, certain difficulty in separating the cells or their microsomes, the danger of a toxic, anaphylactogenic effect, and a probable viral or microbial invasion. This method is similar to the one proposed by Eiseman et al. (1965) for extracorporeal perfusion by the pig's liver; it was tested and fell short of expectations.

(2) *Detoxifying function of the liver reproduced artificially by the use of "artificial cells"* (Chang, 1972) *as microcapsules containing enzymes that ensure the synthesis of urea, the formation of paired sulfoethereal compounds, glucuronides, etc.* This is a very promising way, though obviously difficult, because there is not enough information on the enzymatic organization of the hepatic cell, and it is hard to isolate enough pure enzymes. However, problems of immobilizing and packing enzymes, being important in the creation of "artificial cells," have largely been solved.

(3) *Detoxifying function of the liver reproduced artificially by the creation of an artificial detoxifying-excretory system.* It is now known quite well how the liver detoxifies poisonous hydrophobic compounds that get into the organism from outside in the form of medicine, poisons, and food additives, which are termed xenobiotics. This mechanism is illustrated schematically in Fig. 1. It shows that the main reaction of detoxification in the liver is that of oxidation of xenobiotics on cytochrome P_{450}, which is a special detoxifying enzyme. The essence of this reaction is that the oxidized compound always dissolves better in water,

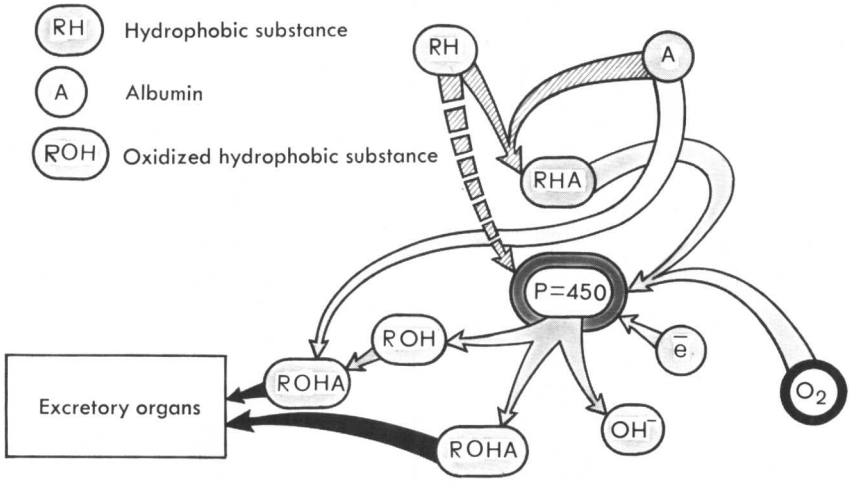

Fig. 1 Mechanism of the oxidation of hydrophobic substances by cytochrome P_{450} (according to Archakov).

and therefore it can be much lighter than the original substance, which is drawn into other metabolic transformations or is removed from the organism by excretory organs. The given scheme shows that the simplest detoxifying cycle is effected by only two biomolecules: albumin and cytochrome P_{450}. Albumin performs the transport function, while cytochrome P_{450} performs the oxidizing function. Hydrophobic substances (RH) that get into the organism from outside combine with albumin and are transported as the RHA complex to the liver. Some of the substances can get into the liver in a free state as well. The xenobiotic is oxidized there on cytochrome P_{450} in the membranes of the endoplasmic network of the hepatocyte, and then it enters, either as the ROHA complex or in a free state (ROH), the excretory organs, from which it is disposed. According to this viewpoint, cytochrome P_{450} performs the principal intoxicating function in the liver with respect to xenobiotics. Its mechanism is illustrated in the simplest form in Fig. 2. Cytochrome P_{450} is a complex protein that consists of two parts: the apoenzyme, or the protein part proper, and the prosthetic group, or the heme. The apoenzyme acts as a receptor, and it is capable of binding hundreds of compounds that are extremely diverse by their chemical structure. The heme is capable of converting molecular oxygen from an inactive form into an active one and using it in oxidation reactions. Following is a list of oxidation reactions catalyzed by cytochrome P_{450} (reactions depending on nicotinamide-adenine dinucleotide phosphate):

I Oxidation of xenobiotics
- (a) Oxidizing dealkylation
  - (1) N dealkylation
  - (2) O dealkylation
  - (3) S dealkylation
- (b) Hydroxylation of
  - (1) Cyclic compounds
  - (2) Aromatic hydrocarbons
  - (3) Cyclic saturated hydrocarbons
  - (4) Heterocyclic hydrocarbons
- (c) Hydroxylation of aliphatic saturated hydrocarbons (alkanes); hydroxylation of alkyl side chain
- (d) Oxidation: formation of
  - (1) N oxides
  - (2) N hydroxylation
- (e) Oxidative deamination
- (f) S oxidation and desulfonation

II Oxidation of natural substrates
- (a) Oxidation of saturated fatty acids
- (b) Hydroxylation of steroids, bile acids, and cholesterol
- (c) Biosynthesis of prostaglandins
- (d) Peroxidation of unsaturated fatty acids
- (e) Hydroperoxidase reactions in microsomes

III Reduction reactions
- (a) Reduction of azo compounds
- (b) Reduction of nitro compounds
- (c) Reducing dehalogenation

There are obviously several dozens of such types, and therefore this enzymatic system affords great opportunities. The only chemical demand made on the structure of the compound being oxidized on cytochrome P_{450} is that it should be hydrophobic—i.e., it should be able to dissolve in fats. In our con-

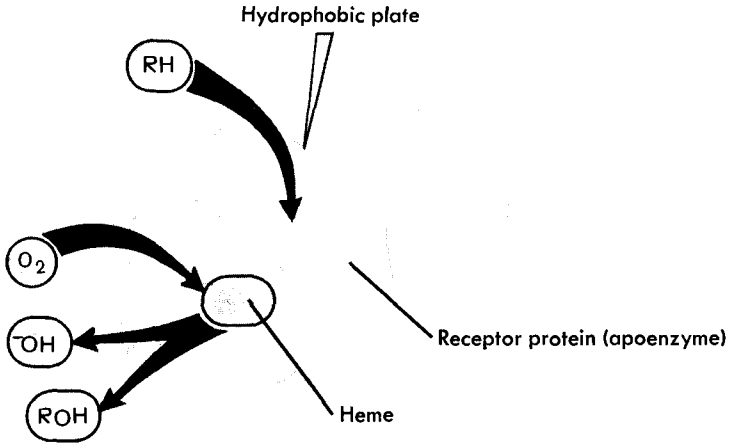

Fig. 2 Schematic illustration of two functional parts of cytochrome P_{450} (according to Archakov).

sideration of the importance of cytochrome P_{450} in detoxification processes, mention should be made of its key role in the reactions of oxidation of xenobiotics and endogenous hydrophobic compounds (cholesterol, bilirubin, bile acids, steroid hormones, etc.) (see accompanying scheme). Consequently, this enzyme can be regarded as the principal detoxifying enzymatic system of the liver. Unfortunately, there are great difficulties in directly using this enzymatic system for detoxification purposes—e.g., in the artificial cell by Chang's method (1972). Cytochrome P_{450} works not on its own, but in the composition of the redox enzymatic chain, supplying it with electrons needed for activating molecular oxygen. Nicotinamide-adenine dinucleotide phosphate (NADP), an expensive metabolite, is used as an electron donor. Moreover, the enzyme is localized in the membranes of the endoplasmic network of the hepatocyte, and its purification is very difficult. Therefore, it is impossible to directly use this enzymatic system for detoxification purposes at present.

Cytochrome P_{450}

↓

Oxidation of hydrophobic substances

Their removal from the cell (detoxification) (1) Xenobiotics (2) Substances of endogenous origin	Biosynthesis and disintegration of biologically active compounds (steroid hormones; prostaglandins)	Biosynthesis and disintegration of compounds that participate in building biomembranes (oxidation of saturated and unsaturated fatty acids; biosynthesis and oxidation of cholesterol)

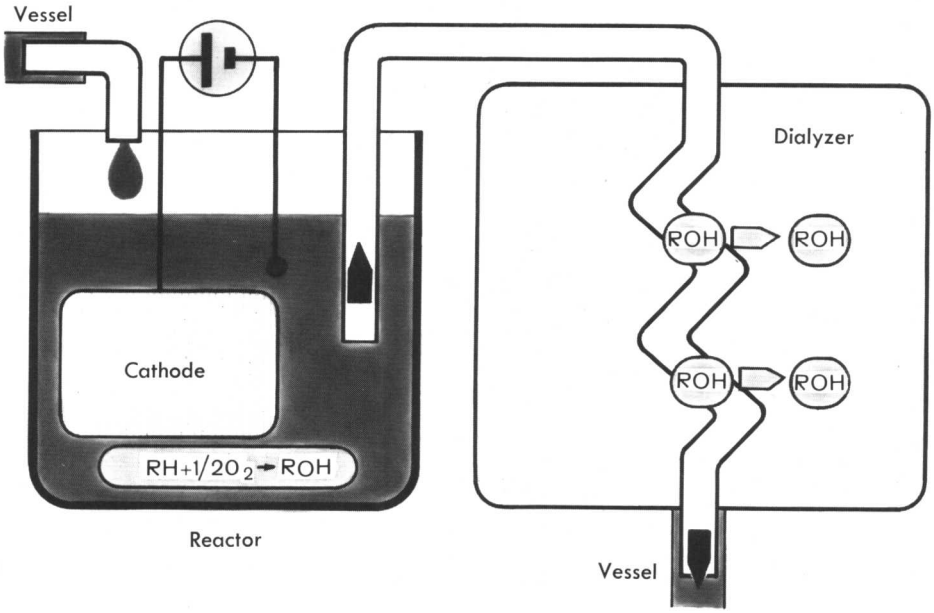

Fig. 3 Model liver-kidney system (according to Archakov).

The detoxifying-excretory system, produced in the Laboratory of Enzymology and Bioenergetics of the Scientific Research Center No. 2 of the Second Moscow Pirogov Medical Institute (Archakov), consists of a reactor, which acts as an oxidizer, and a dialyzer (Fig. 3). Molecular oxygen reduced by electric current on the cathode oxidizes hydrophobic substances in a simple electrochemical system, which, to a certain extent, simulates the oxidizing function of cytochrome P_{450}. The oxidizing reactor simulates the oxidizing function of the liver, while the dialyzer simulates the excretory function of the kidneys. The system proposed is thus a very simple model of the liver-kidney complex, which performs the principal detoxifying function in animals.

(4) *Detoxifying function of the liver reproduced artificially by the use of sorbents to bring about the sorption of xenobiotics and endogenous toxins directly from the blood.* This can be done because of the great achievements made in sorbent chemistry and the clinical and experimental experience gained in using sorbents for hemoperfusion.

The hemosorption system can, with certain allowances, be called an artificial liver or, to be more exact, an artificial liver support system, just as the hemodialysis apparatus is called an artificial kidney (Abel et al., 1913) since it performs one of the most important kidney functions and reproduces the principal kidney mechanism (dialysis).

Two unsolved problems of sorbent chemistry

Among the numerous sorbent chemistry problems dealt with in Chapter 2, two main ones are still not completely solved: (1) adsorbent-blood compatibility