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## Lipid-Absorbing Polymers

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Present medicinal approaches to cholesterol reduction are indirect. They employ ion exchange to bind bile acids (which are derived from cholesterol by the liver) so that they will be eliminated instead of assimilated.

New polymers have been made that have the unusual property of being capable of absorbing both water and oils. As a result of this property, they are able to absorb lipids from micellar solutions. Lipid absorptions from model bile solution as high as 10% (based on dry polymer weight) in 5 min and 59% at equilibrium have been measured. The presence of significant amounts of cholesterol, as well as of bile acid, in the absorbed lipids has been confirmed by thin layer chromatography.

### Introduction

Present medicinal approaches to reducing serum and tissue cholesterol levels in man are indirect. Intestinal reabsorption of bile acids, which are liver-produced derivatives of cholesterol, is reduced by administration of nonabsorbable bile acid-binding polymers. The binding is accomplished by means of ion exchange on polymers bearing amine groups. For example, materials under study include various primary, secondary, and tertiary ethylamine adducts of cellulose and other polysaccharides (Refs. 1,2), a copolymer of tetraethylene pentamine and epichlorohydrin (Ref. 3), and a quaternary ammonium styrene-divinylbenzene copolymer. The last polymer, known as Cholestyramine, has been in use medically for a number of years.

The approach of the JPL work is different in two ways. It aims at removing not only bile acids but also cholesterol itself. The operating mechanism is absorption instead of ion exchange.

An isotropic micellar solution of bile lipids<sup>1</sup> was employed for in vitro measurements of the absorption capacities and absorption rate capabilities of polymers. Henceforth, this solution will be called model bile.

The first polymers tested were representative of those shown in previous work (Ref. 4) to have high capacities for absorbing hydrocarbon materials, including some lipids. All were composed of lightly crosslinked, amorphous hydrocarbon chains from which the sol fraction had previously been extracted. Although the data were unsystematically variable, a result found later to be caused by incomplete removal of the sol (or nonnetwork) fraction from polymer samples, there was sufficient evidence for the conclusion that these hydrocarbon polymers were incapable of absorbing significant amounts of bile lipids from micellar solutions. In addition, it was found that the model bile solution could extract lipids from polymers.

### **Micelle-Polymer Interaction**

The failure of oleophilic polymers as absorbers for lipids from micellar solutions led to the proposition that a successful polymer must be composed of a mixture of both oleophilic and hydrophilic chains. The basis for this theory is the higher affinity of lipid polar groups for water, as demonstrated in these experiments, over that of their larger aliphatic parts for the hydrocarbon polymer chains. High polar group-water affinity is the force also that makes possible the solution of high concentrations of properly proportioned lipids in water. In such solutions water is the continuous phase, and all of the lipid molecules are in micelles that are submicroscopic clusters arranged so that the large hydrocarbon tails of the molecules are surrounded by a sheath composed of their polar groups.

The interaction between micelles and hydrocarbon polymers that might be expected on the basis of the above discussion would be limited to the polymer surface. Lipid molecules coming into close contact with polymer chains will be unable to diffuse into the polymer because of the force retaining the polar groups in the aqueous phase. At equilibrium a polymer particle probably would resemble a very large micelle, a hydrocarbon body surrounded by a polar sheath. Therefore, for a polymer to be able to absorb larger amounts of bile lipids, it must be able to absorb water, as well as oils, so as to attract both parts of lipid molecules.

### **Polymer Preparation and Composition**

The general scheme for preparing oil-absorbing urethane-cured polymers described previously (Ref. 4) was used. Formulations were calculated to

<sup>1</sup> In human bile, the lipids, bile salt, lecithin, and cholesterol in proportions ranging around 60.7%, 33.7%, and 5.6%, occur as 8.9% total lipids in water. The model bile solutions used in this work contained 45.5% total lipids distributed as 54.9% sodium cholate, 44% crude egg lecithin, and 1.1% cholesterol. This departure in composition was necessary for the preparation of stable, homogeneous, isotropic micellar solutions using available ingredients. Lack of lecithin purity is believed to be the cause of the impossibility of obtaining stable representative compositions. Cholesterol concentration, based on total solution, is the same, however.

yield low levels of crosslinking. Prepolymers and other ingredients were dissolved, in formulated proportions, in a solvent. The mixtures were cured by heat. After cure, sol (or nonnetwork) fractions were removed by repetitive extraction. To obtain accurate lipid absorption capacity measurements, it was found necessary to approximately double the number of fresh extractions. Thin layer chromatography (TLC) was adopted as a measure of extraction effectiveness.

Because of their high water solubility and their suitability for use in urethane systems, hydroxyl-terminated polyethylene oxide (PEO) prepolymers were selected to contribute hydrophilic chains in polymeric mixtures with the previously used oleophilic polybutadiene (PB) prepolymers. Dioxane was found to be an appropriate solvent for dissolving the prepolymers and in which to produce cured, homogeneous, mixed-chain polymers. Polymers were prepared with several weight ratios of the two kinds of prepolymers: parts PEO to parts PB of 100/0, 90/10, 75/25, and 0/100, each with appropriate amounts of curing ingredients.

### **Measurement of Lipid Absorption**

Polymer samples were used in two particle size classes for lipid absorption tests: chunk (about 6 mm) and ground (about 1 mm). Contact times for polymer samples with model bile ranged from 5 min to 220 h. Samples were weighed before contact, after contact, and after subsequent removal of absorbed water by vacuum drying.

### **Results**

The maximum absorptions that were measured were obtained with polymer No. 806, which is composed of 75 parts PEO and 25 parts PB plus curing ingredients. Total absorption (water plus lipids) at equilibrium measured on a number of samples of this type of polymer ranged from 305 to 309%, based on original polymer weight. Lipid absorption (measured after removal of absorbed water) measured from 57 to 59.4%. These measurements were made after from 140 to 150 h of contact. After 5 min, the corresponding values were 54.2 to 59.8% total and 4.1 to 10.8% lipids.

The particle size effects on absorption rate expected from diffusion considerations were observed in all comparisons between chunk and ground samples. Chunk absorption was slower. Rate measurements also indicated that in the earlier time periods water absorption leads lipid absorption. The water and lipid absorption rates in ground polymer No. 806 (75/25 PEO/PB) are illustrated in Fig. 1.

Absorbates extracted from representative samples that had absorbed significant amounts of lipids were shown by thin layer chromatography (TLC) to contain all three lipids: cholesterol, sodium cholate, and lecithin. No quantitative measurement of the relative concentrations of these three compounds were made; however, qualitative examination of the TLC

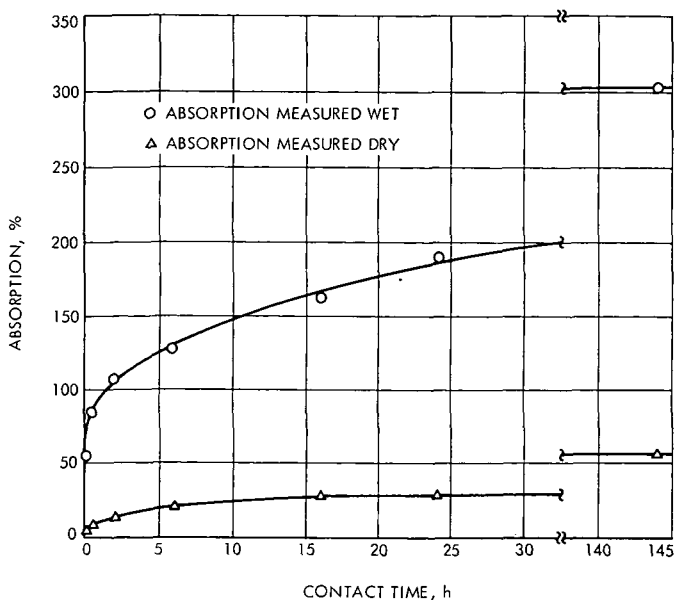


Fig. 1. Rate of absorption of model bile by ground polymer No. 806

records indicate that they are probably in about the same proportions as they were in the model bile solutions. A TLC record confirming cholesterol absorption in polymer No. 806 (75/25 PEO/PB) is shown compared with a standard in Fig. 2.

The absorption capacity of polymers for lipids from micellar solutions is highly dependent upon polymer structure. This result is illustrated in Fig. 3. In 147 h, polymer No. 720 (100/0 PEO/PB) absorbed 271% total material, but, after the water was removed, only 0.3% lipid residue remained. In 144 h, polymer No. 800 (0/100 PEO/PB) absorbed only 3% total, 2/3 of which was lipid. In corresponding contact times, polymers with intermediate compositions, No. 734 (90/10) and No. 806 (75/25), absorbed much more lipid, 9.5% and 59% respectively. Reliable data are not available for polymers whose compositions lie between PEO/PB ratios of 75/25 and 0/100 because of difficulties in grinding these more rubbery materials in the laboratory. This obstacle will be eliminated in future work, and it can be expected from the data in Fig. 3 that higher absorption capacities will be measured.

## Conclusions

The results of these experiments permit the following conclusions:

- (1) While crosslinked polyethylene oxide (PEO) polymers will absorb water and crosslinked polybutadiene (PB) polymers will absorb lipids, neither polymer will absorb appreciable amounts of lipids from micellar solutions of lipids-in-water.

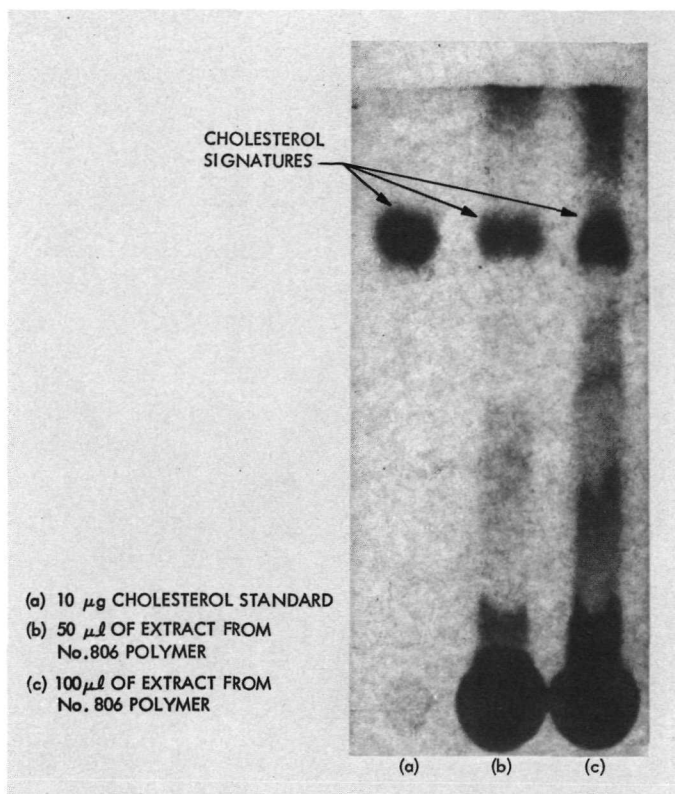


Fig. 2. Thin layer (TLC) chromatograph showing cholesterol in absorbate from polymer No. 806

- (2) Crosslinked, amorphous polymers composed of homogeneous mixtures of PEO and PB chains will absorb significant amounts of lipids from micellar solutions.
- (3) The lipid absorption capability of mixed chain polymers is markedly dependent on the relative proportions of oleophilic and hydrophilic chains in the polymer. Whereas the highest absorption measured was 59.4% lipid (based on original polymer weight) in a 75/25 PEO/PB polymer, trends in the data indicate the probability that higher capacities will be found in compositions between 75/25 and 0/100 PEO/PB.
- (4) Short-term absorption capacity can be improved by reduction in polymer particle size. Almost 24 h were required for a 75/25 PEO/PB polymer in chunk form ( $\sim 6$  mm) to absorb the 10% achieved in 5 min by the same polymer ground to  $\sim 1$  mm size.
- (5) All three lipids used to make the micellar test solutions, cholesterol, sodium cholate, and lecithin, were found in absorbates. There was no evidence of selectivity related to lipid structure.

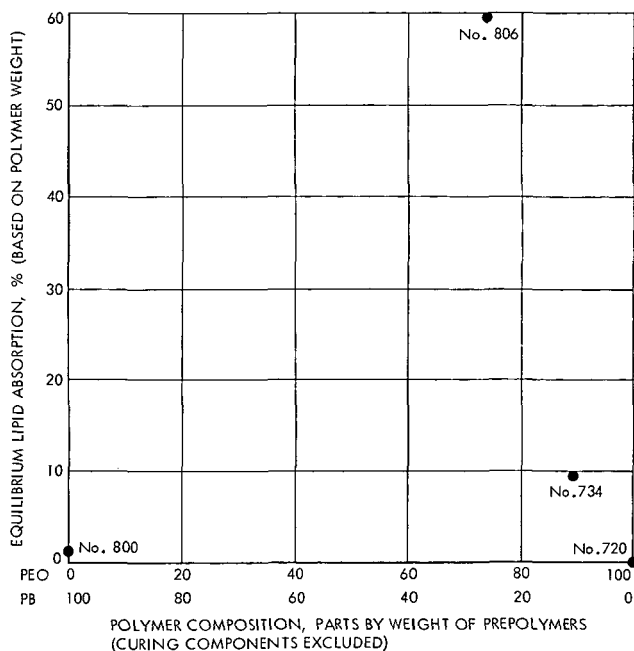


Fig. 3. Relationship between polymer structure and micellar lipid absorption

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