

A STUDY OF THE TOXIC PROPERTIES OF RUSSIAN CELLOPHANE FILM FOR THE "ARTIFICIAL KIDNEY" APPARATUS

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Every year the artificial kidney is more widely used. However, it must be remembered that this method may cause death if it is carried out without due observance of the necessary conditions. Among the possible complications Rosenak has correctly included the liberation of toxic products of the cellophane sheet or tube through which the patient's blood was circulating during hemodialysis. The possibility of a serious toxic effect from this cause becomes clear when we consider that 55-90 liters of blood undergoes dialysis in the apparatus in six hours and that the area of thin film over which the blood is spread is 16,000-22,000 cm².

Skeggs and his co-authors were the first to draw attention to this point and to point out that if untreated cellophane is used in experiments on dogs, a marked depressor reaction occurs. Taddei and Mosetti [5] pointed out that toxic products could be formed in the cellophane. They injected an extract of cellophane film intravenously into the rabbits, and showed that it caused death within four hours. This occurred in association with a marked fall in blood pressure. At the symposium on chemodialysis (1958) the problem was further discussed by Toussaint, Verbanck and Telerman [6]. They showed that with various modifications of the Kalf-Wachinger artificial kidney in which untreated cellophane was used originally, a fall in blood pressure occurred. Even quite a short session frequently terminated in death.

Evidence that these effects are not due to the direct action of impurities from cellophane on blood is provided by the fact that after the cellophane has been carefully worked and boiled the depressor response no longer occurs.

In experiments on hemodialysis Maher et al. have shown that a severe shock reaction in dogs occurs even when the cellophane has been boiled for a long time. However, in this case the reason for the reaction appears to be that insufficient attention had been paid to the matching of the donor blood with that of the recipient.

Many indications have been published concerning the unfavorable action of cellophane on the formed elements of the blood. In work with the "artificial kidney" apparatus a leukopenia and a marked fall in the number of thrombocytes is a constant feature. This fact has been emphasized by Rosenak who showed that in one of his patients in whom a hemodialysis had been carried out three times, the number of thrombocytes fell to 5,000, which led to a fatal internal hemorrhage. Many observations have led to the view that the occurrence of leukopenia in hemodialysis is at any rate in part due to the chemotactic influence of the cellophane on the leukocytes. It is important to realize that impurities in the cellophane may themselves cause hemolysis [1].

In connection with the creation of a Russian "artificial kidney," for which cellophane film is essential, we decided to test our own commercial cellophane to find whether it contains substances exerting a hypotensive effect or any other toxic action and to determine the effect of the cellophane film on the elements of the blood.

EXPERIMENTAL METHOD

We used two types of cellophane film; the usual type used in the food industry and issued by the Klinskii works; in this kind glycerin is used as a plasticizer. The second type of cellophane was made to our order by No. 512 Combine in which glucose was used as the plasticizer. Cellophane sheet measuring 20,000 cm square was cut up into small portions and 50-70 ml of a concentrated aqueous extract was made from it.



Influence of a cellophane extract on the arterial pressure of a dog. Curves, from top to bottom; arterial pressure (record from mercury manometer), line, time marker.

The experiments were carried out on healthy dogs under morphine and hexenal anesthesia. They received 10-20 ml of the extract intravenously. It was injected several times at intervals of 30 min. During the experiment electrical or mercury-manometer records were made of the blood pressure in the femoral artery, and the respiration rate was measured.

To determine the influence of the cellophane extract on the formed elements of freshly collected heparinized canine blood, we poured it into beakers. To one we added a finely divided untreated cellophane, to the second we added the same amount of cellophane which had been boiled for three hours, while the third served as control. The vessels were placed in a refrigerator at 4°. After two hours samples were collected from each beaker, a count of the blood cells was made, and the amount of free hemoglobin in the plasma determined in the usual way.

EXPERIMENTAL RESULTS

Injection of cellophane extracts of either type caused no change of arterial pressure (see figure), pulse frequency, or ECG; neither was there any change in the frequency of the respiration, and breathing was not affected in any way. During the experiment and after the operation there were no toxic manifestations.

These investigations have established that contact of cellophane sheet with blood induces no changes (with respect to a control animal) in any of the indices studied. This is clear from the table giving the results of one experiment.

We may, therefore, suppose that unlike certain foreign brands of cellophane, our own variety exerts no marked toxic action. We must point out that in our experiment, to obtain the extracts, we took an amount of cellophane which was far greater than the amount required for any existing type of artificial kidney.

There is, therefore, every reason to suppose that the absence of any hypotensive action must be due exclusively to the qualities of the cellophane sheet itself. This finding was subsequently confirmed by the use of an artificial kidney on healthy animals. In these experiments we used cellophane (with glucose as a plasticizer) which had undergone no preliminary treatment. During the course of a dialysis lasting four hours practically no changes occurred.

Changes in Blood on Contact with Cellophane

Index	Control		Cellophane	
	before experiment	at 4°	treated	untreated
Number of erythrocytes	5,670,000	5,190,000	4,940,000	5,780,000
Number of leucocytes	9,650	8,650	8,850	8,555
Number of thrombocytes (as %)	15	2	2	1
Amount of hemoglobin in plasma (in mg %)	14	80	27	83

No unfavorable influence on blood pressure or on the course of dialysis was noticed. At the end of the experiment the extent of the hemolysis was not large (not more than 30-40 mg % every 4-6 h period). When a hemodialysis was carried out on a human subject whose erythrocytes are less fragile than those of the dog, the hemolysis was no more than 7-12 mg%.

As far as the number of leucocytes and thrombocytes is concerned, like other authors we found that in the first few hours of the dialysis the number of leucocytes fell by 55-90%, and the number of thrombocytes by 76-93%. However, these changes were not irreversible. Immediately after the end of the dialysis, or one day later, the leucocytes and thrombocytes in the dog regained their original number or even exceeded it.

It is important that cellophane film is strongly selective in what proteins and other substances of large molecular weight it lets through. A film which passes protein cannot be used for hemodialysis. All samples of cellophane were, therefore, tested for protein permeability. The test was made with sulfosalicylic acid, and showed that the samples of cellophane available to us did not let through protein.

The facts reported above allow us to recommend cellophane of Russian manufacture for use in the "artificial kidney" apparatus. Preference should be given to cellophane made with a physiological plasticizer such as glucose.

SUMMARY

Experiments with intravenous injections of an aqueous extract of cellophane sheet into dogs showed that there were no significant changes in the blood pressure or respiration, nor any disturbances of the animal's general condition. It was found by experiments in vitro that Soviet cellophane membrane caused no significant changes in the blood cells and was impermeable to protein molecules.

Soviet cellophane membranous sheet may, therefore, be recommended for use in the artificial kidney apparatus.

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