

PREPARATION AND EXCHANGE PROPERTIES OF CATION EXCHANGE RESIN MIXTURES FOR THE REMOVAL OF EXCESSIVE AMMONIUM FROM THE EXTRACORPOREAL CIRCULATION SYSTEM

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Summary: The polystyrene sulphonic acid strong cation exchange resins were found to be more efficient in ammonium removal compared to the phenol sulphonic acid and carboxylic acid resins. However, no one form (sodium form, potassium form, calcium form, magnesium form) of the Amberlite IR-120 resin used was considered suitable for extra-corporeal circuits, because, in each case, drastic changes occurred in the concentrations of other cations, particularly K^+ , Ca^{++} and Mg^{++} , of the effluent artificial serum. In order to overcome these defects, various resin mixtures ('B', 'C', 'D', 'E', 'F' and 'G') of the four resin forms were worked out from the relative affinity of each resin form for the cations of the artificial serum. These resin mixtures were found to be better and more suitable for extracorporeal circuits compared to the mixture of two resin forms of Ching and associates (3) and slurried resins of Kissack and associates (15). From the exhaustion studies it was found that for the optimum ammonium removal, fresh resin mixture columns should be substituted in the circuits after five liters of the artificial serum (or blood) have been passed. The final resin mixture 'G' (750 meq) was found to remove 90% of ammonium from the artificial serum without any appreciable changes in the concentration of its other cations. This resin mixture was concluded to be the ammonium specific resin for the safe use in the extra-corporeal circulation system.

INTRODUCTION

Ion exchange resins are being used in the extra-corporeal circuits for the treatment of hyperammonemia of hepatic failure (3, 12-16, 18, 19, 23, 24) and hyperkalemia of renal failure (6, 17, 25). The sodium form of the strong cation exchange resin has been employed by the various authors, both experimentally and clinically, for the correction of ammonia intoxication associated with hepatic failure. This resin, though effective in extracting ammonia, was found to sequester other cations of the blood such as calcium, potassium and magnesium, resulting in the development of a dangerous hypocalcemia, hypokalemia and hypomagnesemia. There have been no satisfactory methods available for effectively correcting these deficiencies associated with ion-exchange perfusions. The present work was undertaken to modify the cation exchange resins by detailed *in vitro* studies, for their safe use in the extracorporeal circulation system. Results of the preliminary studies have been reported earlier (2, 7, 8, 26).

MATERIALS AND METHODS

Preparation of cation exchange resins: Cation exchange resins used were selected from different types of commercially available analytical grade resins (Table I). Amberlite resins, manufactured

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by Rohm and Hass Company, Philadelphia, U.S.A.; Zeokarb resins, manufactured by Permutit Company, London, U.K. and Dowex resins, manufactured by Dow Chemical Company, Midland, U.S.A., were utilized.

TABLE I: Particle size, moisture content and exchange capacities worked out for various types of resins.

<i>Commercial name</i>	<i>Type</i>	<i>Functional group(s)</i>	<i>Resin fraction(s) (B.S.S.) selected for study</i>	<i>Moisture content (%) of the air dried hydrogen form</i>	<i>Exchange capacity (meq per g. dry resin (110°C))</i>
Amberlite IR-120	Cross-linked Polystyrene	—SO ₃ H	22/30, 44/60	25.73	5.075
Amberlite IR-200	Cross-linked Polystyrene	—SO ₃ H	22/30	24.11	4.77
Zeokarb-225	Cross-linked Polystyrene	—SO ₃ H	22/30	27.61	5.54
Dowex-50x8	Cross-linked Polystyrene	—SO ₃ H	22/30	26.11	4.60
Zeokarb-215	Phenol Sulphonic acid	—OH; —SO ₃ H	22/30	20.92	2.592
Amberlite IRC-50	Cross-linked methacrylic acid	—COOH	33/44	15.02	10.752

The polystyrene sulphonic acid strong cation exchange resins have been mainly used. These resins contain only one ion active group i.e. -SO₃H, which makes them mono-functional and strongly acidic. Cross linkage is provided by 8-10% divinyl benzene content and their ion exchange capacity remains the same for all pH values. Furthermore, these have extremely hard, spherical and smooth surfaced particles which remain stable up to 120°C and hence can be easily sterilized for extracorporeal circuits. These particles are also non-hemolytic and the residue due to resin solubility was never found to be more than 0.3 mg per 100 ml of the solvent for 10 g of the resin (7).

All the resins were completely cycled four times between the sodium and hydrogen forms, by infinite bath method, using pyrex glass columns, 1 meter long and 5 cm in diameter and fitted with sintered glass filtered at the proximal end. Influent for cycling were 5% NaCl and 2N HCl solutions. It was found necessary to cycle these resins at least three times to completely drive out organic impurities from the pores of these resins. The final hydrogen forms were then thoroughly washed with deionized water until the washings were completely free from acid. The resins were then removed from the glass columns and surface dried in a current of air at about 35-40°C. The resins were then allowed to come into equilibrium with atmospheric humidity by spreading them in one-particle deep layers in large filter paper trays for about a week. This was done to ensure uniformity of moisture content in the resin particles and also to make the resins stable for weighing.

The air dried resins were sieved to give a series of British Standard Sieve (B.S.S.) fractions. Mean swollen particle size of the 22/30 and 44/60 B.S.S. fractions of the Amberlite IR-120 resin, was determined under a microscope fitted with a calibrated micrometer eye piece.

The exchange capacities (in *meq*) of these resins for sodium ions, were determined by shaking intermittently for 48 hours, 1 g samples of the air dried hydrogen form of the resin with 100 ml portions of a mixed solution of 0.1N NaOH and 0.9N NaCl, in 250 ml ground glass stoppered flasks. 25 ml of the equilibrium solutions were withdrawn and titrated for the excess base. Moisture content of the air dried resins was determined by heating the resins at 110°C to a constant weight.

The B.S.S. fraction selected, moisture content and exchange capacities for the various resins are shown in Table I.

The sodium form of the resin was prepared by passing 5% solution of NaCl at progressively decreasing flow rate (1 ml/min after 1 hr) through a column containing desired amount (in *meq*) of swollen particles of the hydrogen form of the resin, until the overnight effluent was of the same pH as that of influent. The sodium form of the resin was then washed thoroughly with deionized water to completely free it from any adhering sodium chloride. Potassium, calcium and magnesium forms of the resin were prepared in the same manner with 5% solutions of KCl, CaCl₂ and MgSO₄ respectively.

Preparation and passage of artificial serum: Artificial serum was prepared by the method of Hald (6). It was made hyperammonemic by the addition of 100 µg NH₃-N/100 ml as (NH₄)₂ SO₄. Five litres of the artificial serum which approximates to the blood-volume in adult man, was passed through a column, containing a known quantity of resin or resin mixture, at a flow rate of 20 to 60 ml/min. The apparatus used and details of the procedure have been reported earlier (2). One liter samples of the effluent were collected, in each case, and both the influent and effluents were analysed for various cationic constituents and pH. Calculated mean values for the 5 l effluents were recorded. To have an additional check on the analytical techniques, 50 ml specimen from each of the five, one liter portions, of the effluent artificial serum in each case were mixed together. This mixture was again analysed for the various cationic constituents and pH and the results were found to be in agreement with the calculated mean values.

Exhaustion studies: Exhaustion studies were carried out to find out the maximum capacity of the resin mixtures to take up ammonium from the artificial serum. After passing 5 l (first portion) of the artificial serum through a particular resin mixture, another fresh 5 (second portion) of the artificial serum was passed through the same resin column. The ammonium concentration in both the first and the second portions of the influent artificial serum was 100 µg NH₃-N% equivalent to the absolute quantity of 5000 µg NH₃-N respectively.

Studies on slurry technique: Mixed sodium-calcium-potassium forms of the strong cation exchange resin were prepared according to Kissacks *et al.* (15). Four portion, each

of 100 g (capacity equivalent to 377 meq), air dried, sodium form of the strong cation exchange resin, Amberlite IR-120, B.S.S. 22/60, were kept in contact with deionized water overnight. The swollen particles of each portion were then quantitatively transferred to 500 ml flasks for treatment with the slurry solutions. 200 ml of the slurry solution was used for each flask. The concentration of calcium chloride in the slurry solution was kept constant at 3% (equivalent to 109.15 meq of Ca^{++}) for each flask. The concentration of potassium chloride in flasks I, II, III and IV was 1%, 0.5%, 0.4% and 0.25% equivalent to 26.26, 13.13, 10.66 and 6.665 meq of K^+ respectively.

The supernatant liquid from each flask was decanted after an equilibrium period of 48 hours, and analysed for sodium, calcium and potassium concentrations. The slurried resins, remaining in the flasks, were washed with deionized water and quantitatively transferred to the resin columns for the passage of the artificial serum.

Ammonium was determined by the microdiffusion method (5); sodium, potassium and calcium were estimated by standard analytical techniques (27) and magnesium by the titan yellow method (20).

RESULTS

Effect of type of resin: Fig. 1 shows the mean absolute values for the ammonium uptake. It is seen that polystyrene sulphonic acid resins are more efficient in the ammonium removal com-

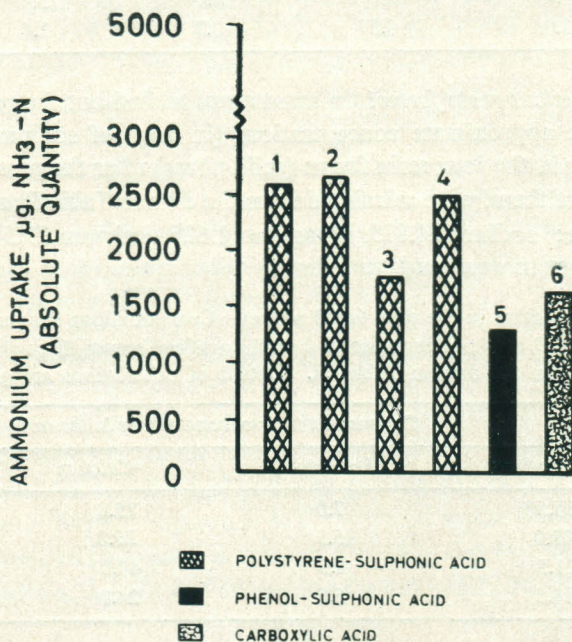


Fig. 1: Effect of type of resin on the uptake of ammonium from 5 l of the artificial serum containing 5000 µg. $\text{NH}_3\text{-N}$.

- (1) Amberlite IR-120, (2) Amberlite IR-200, (3) Zeokarb 225, (4) Dowex 50x8, (5) Zeokarb 215, (6) Amberlite IRC-50.

pared to the phenol sulphonic acid and carboxylic acid resins. Hence all the subsequent experiments were carried out with polystyrene sulphonic acid resins and out of this group, Amberlite IR-120 was selected.

Effect of form of resin: The results are shown in Table II. It is seen that all the four forms of the resin are almost equally efficient for the removal of excessive ammonium. However, the picture of other cations is very much different with the different forms of the resin. Marked cationic concentration changes were brought about by each form of the resin affecting seriously the levels of potassium, calcium and magnesium in the effluents. Therefore, no single form of the resin seems to be suitable for the removal of ammonium from blood by extracorporeal perfusion.

TABLE II: Effect of form of resin on the ammonium uptake and on other cations of the artificial serum (Mean values for 5 l artificial serum).

Cation	Influent artificial serum	Effluent artificial serum			
		Sodium form	Potassium form	Calcium form	Magnesium form
Ammonium $\mu\text{g. NH}_4\text{-N\%}$	100.0	48.5	46.2	48.5	51.0
Sodium meq/l	138.0	143.6	135.6	133.7	135.1
Potassium meq/l	4.1	2.7	13.8	2.8	3.0
Calcium meq/l	5.0	0.0	0.0	13.4	0.2
Magnesium meq/l	2.0	0.5	0.7	1.4	9.8

Effect of mixture of various resin forms: In an attempt to find out the proportion of different forms in the mixture, the approximate concentrations (in meq) of sodium, potassium, calcium and magnesium remaining in the four resin forms (solid phase) after the passage of 5 l of the artificial serum through each of them, were calculated from the data in Table II, and their average concentrations in (meq) were: sodium 24.875, potassium 8.625, calcium 29.5 and magnesium 12.0 (Table III). These calculations were made as follows:

TABLE III: Concentration of cations in the resin (solid phase). Concentrations (in meq) of various cations in the resin (total of 75 meq), after passing 5 l of the artificial serum through the different resin forms, were calculated from the data in Table II. Details of calculations are given in the text.

Resin form	Cations and their concentrations in the resin			
	Sodium	Potassium	Calcium	Magnesium
Sodium Form	35.5*	7.0	25.0	7.5
Potassium Form	28.0	15.5*	25.0	6.5
Calcium Form	21.5	6.5	44.0*	3.0
Magnesium Form	14.5	5.5	24.0	31.0*
Total for the four resin forms	99.5	34.5	118.0	48.0
Average (Total $\times \frac{1}{4}$)	24.875	8.625	29.5	12.0

* From difference of 75 meq and the total of the rest three.

With the use of sodium form of the resin, the absolute amounts of decrease of potassium, calcium and magnesium in the effluent artificial serum were: 7.0, 25.0 and 7.5 *meq* respectively; the total of these comes to 39.5 *meq*. This total amount had been taken up by the sodium form of the resin in exchange of its sodium released into the effluent artificial serum. The amount of sodium in the resin after this experiment would be 75 *meq* minus 39.5 *meq* i.e. 35.5 *meq*. Therefore, the amounts of sodium, potassium, calcium and magnesium in the resin after passing 5 l of the artificial serum through the sodium form of the resin would approximately be 35.5, 7.0, 25.0 and 7.5 *meq* respectively; total being 75.0 *meq*. Similar calculations were made from the results of the experiments carried out with the Potassium, calcium and magnesium forms of the resins (Table II). The calculated values for the four resin forms are given in Table III.

However, in the first instance the following mixture 'A' of the resin forms was tried (in *meq*): sodium 23, potassium 12, calcium 30 and magnesium 10, total 75 *meq*. These resin forms were separately prepared from hydrogen form of 22/30 B.S.S. fraction of IR-120 and after washing with deionized water, they were mixed and quantitatively transferred to the column. Concentrations of the cations in 5 l of the artificial serum after passing through this mixture of resin forms were: ammonium 55 $\mu\text{g NH}_3\text{-N}/100\text{ ml}$, sodium 134 *meq/l*, potassium 5 *meq/l*, calcium 4.6 *meq/l* and magnesium 3.6 *meq/l*. The amounts of potassium, calcium and magnesium in the solid phase (resin) after passing 5 l of the artificial serum through the resin forms mixture 'A' as calculated from the above results were 7.5, 32.0 and 2.0 *meq* respectively; total being 41.5 *meq*. The amount of the resin in terms of capacity was 75 *meq* and therefore, the amount of sodium in the resin would be 75.0 minus 41.5 i.e. 33.5 *meq*. On the basis of these calculations the next mixture of the resin forms, mixture 'B' to be tried was as follows (in *meq*): sodium 33, potassium 8, calcium 32 and magnesium 2, total 75 *meq*.

The results after passage of 5 l of the artificial serum through this mixture 'B' are shown in Table V. As is seen, 48% of ammonium is removed from the influent artificial serum without any significant changes in its other cationic concentrations. The pH of the effluent was 6.1 against 6.0 of the influent artificial serum.

EXPERIMENTS WITH RESIN MIXTURE 'B':

Effect of particle size: Further experiments with the resin mixture 'B' were carried out to find out the effect of particle size on the uptake of ammonium. Two fractions of the resin used for preparing the mixture 'B' viz. B.S.S. 22/30 with particle size of 0.95 mm and B.S.S. 44/60 with particle size of 0.75 mm. Results of passage of the artificial serum showed no significant difference between the two fractions and ammonium removal was 48% and 44% respectively. Subsequent experiments were, therefore, carried out using resin fraction of 22/60 (B.S.S.) air dried, Amberlite IR-120 resin.

Effects of quantity resin mixture 'B': Various quantities (in *meq*) of the mixture 'B' studied were: BX1, BX2, BX4 and BX10 respectively. The mean values for ammonium uptake by the various quantities from 5 l of the artificial serum were worked out and percentage uptake of

ammonium was plotted against the various quantities on a log scale. As seen in Fig. 2, a linear regression line could be fitted to all the points which suggested that the relationship between the two is parabolic.

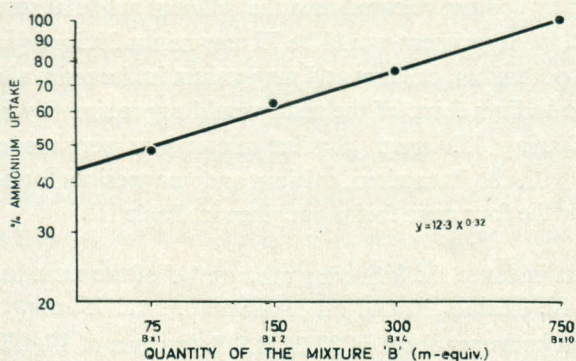


Fig. 2: Effect of various quantities of the mixture 'B' on the uptake of ammonium from the artificial serum (log scale). 5000 μg $\text{NH}_3\text{-N}$ in 5 l of the influent artificial serum is expressed as 100%.

Complete removal of ammonium was achieved by 750 meq (BX10) quantity of the mixture 'B'. However, changes in the concentrations of various other cations particularly potassium did occur. With the mixture BX4 (300 meq), potassium concentration of the artificial serum increased from 4.1 to 7.8 meq/l whereas the sodium concentration decreased from 138.0 to 134.9 meq/l; with the mixture BX10 (750 meq), these changes were more marked, potassium increased from 4.1 to 13.8 meq/l whereas sodium decreased from 138.0 to 126.5 meq/l.

TABLE IV: Composition of various new resin mixtures.
(meq)

Resin form	Mixture 'C'	Mixture 'D'	Mixture 'E'	Mixture 'F'	Mixture 'G'
Sodium	66.2	147	228.0	296.65	380.30
Potassium	11.6	12	12.0	17.35	18.15
Calcium	66.8	130	195.5	265.0	327.95
Magnesium	5.4	11	14.5	21.0	23.60
Total	150.0	300	450.0	600.0	750.0

To overcome this difficulty of the cationic concentration changes when quantities of various forms of the resin were increased, new mixtures of the various resin forms and of different quantities were worked out after making experiments on the lines described already.

The quantities of the new mixtures (C, D, E, F, and G) and proportion of the various forms of the resin in them are described in Table IV. The mean values for the results of passing 5 l of the artificial serum (20 ml/min) through them are shown in Table VI. It is seen from these results that

increase in the quantity of the resin mixture resulted in increased uptake of ammonium from the influent artificial serum. The absolute quantity of ammonium taken up by the resin mixture 'G' was calculated to be 4500 μg $\text{NH}_3\text{-N}$, which was optimum for these sets of experiments. No significant changes were observed in the other cations of the effluent artificial serum with the use of these mixtures (Table V).

TABLE V. Effect of various new resin mixtures of different quantities on the uptake of ammonium and on other cations of the artificial serum. (Mean values for 5 l artificial serum).

Cation	Influent artificial serum	Effluent artificial serum					
		Mixture 'B'	Mixture 'C'	Mixture 'D'	Mixture 'E'	Mixture 'F'	Mixture 'G'
Ammonium μg . $\text{NH}_3\text{-N} \%$ meq/l	100.0	52.0	35.1	25.2	19.0	12.0	10.0
Sodium meq/l	138.0	137.5	136.9	137.14	136.43	137.55	137.9
Potassium	4.1	4.63	4.52	5.0	4.42	4.38	4.09
Calcium meq/l	5.0	5.0	4.86	5.34	5.31	4.9	5.2
Magnesium meq/l	2.0	1.8	1.8	1.86	2.05	2.0	1.84

Exhaustion studies: The results for the resin mixture 'G' are shown in Fig. 3. As seen, there is a low uptake of ammonium from the second 5 l portion (1900 μg $\text{NH}_3\text{-N}$) of the artificial serum as compared to the first 5 l portion (4500 μg $\text{NH}_3\text{-N}$). Therefore, the total of the absolute quantity of ammonium taken up from both the portions was also low (6400 μg $\text{NH}_3\text{-N}$). The same resin mixture was used for both the 5 l portions of the artificial serum. This would be expected, because, the resin mixture already contained ammonium absorbed on it (as a result of the passage of first 5 l portion) when the second 5 l portion was passed. The absorbed ammonium on the resin would tend to be eluted by the cations of the second 5 l portion of the artificial serum. However, with the use of two fresh columns of the resin mixture 'G' for separate passage of the two 5 l portions of the artificial serum, the total of the absolute quantity of the ammonium taken up would be double the amount taken up from the first 5 l portion (9000 μg $\text{NH}_3\text{-N}$).

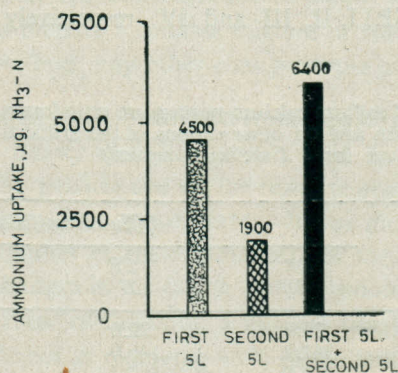


Fig. 3: Exhaustion studies for ammonium uptake by the resin mixture 'G'.

STUDIES ON SLURRY TECHNIQUE:

The amounts of sodium, calcium and potassium in the 200 ml of the slurry solution after equilibrium for 48 hours with the resin were calculated from their concentrations found by analysis. From these results (Table VI) the quantities of sodium, calcium and potassium in the resin, after equilibrium for 48 hours with the slurry solution, were calculated. As an example, in flask I, 377 meq of the sodium form of the resin was slurried with 200 ml of the slurry solution containing 109.15 meq of calcium and 26.26 meq of potassium.

After slurry (equilibrium) for 48 hours the quantities of sodium, calcium and potassium in 200 ml of the slurry solution were 131, 3.4 and 3.54 meq respectively. This means that 131 meq of sodium came out of the resin into the slurry solution in exchange for 105.75 meq of calcium and 23.12 meq of potassium. The quantity of sodium remaining in the resin after equilibrium for 48 hours would be $377 - 131 = 246$ meq. Therefore, the quantities of sodium, calcium and potassium in the resin after the equilibrium in the case of flask I would be 246, 105.75 and 23.12 meq respectively. Similar calculations of after slurry (equilibrium) composition of the resins in the case of flasks II, III and IV were made (Table VI).

TABLE VI: Total quantity of the cations (meq) present in the slurry solution (Liquid Phase) and the calculated quantity of the cations present in the resin (Solid Phase) after equilibrium for 48 hours.

Flask No.	Sodium		Calcium		Potassium	
	LP	SP	LP	SP	LP	SP
I	131.0	<u>246.0</u>	3.4	<u>105.75</u>	3.54	<u>23.12</u>
II	118.5	<u>208.5</u>	3.0	<u>106.15</u>	1.85	<u>11.48</u>
III	112.8	<u>264.2</u>	5.8	<u>103.35</u>	1.54	<u>9.12</u>
IV	111.0	<u>267.0</u>	5.7	<u>103.45</u>	1.0	<u>5.71</u>

Composition of the slurried resin, of each flask, is underlined.
LP = Liquid Phase; SP = Solid Phase.

The results of passage of the artificial serum (60 ml/min.) through the various slurried resins of different flasks i.e. slurried resin (SR) I, II, III and IV respectively (Table VI), are given in Table VII.

TABLE VII: Effect of four different mixed sodium-calcium-potassium resin forms, prepared by the slurry technique, on the uptake of ammonium and on other cations of the artificial serum.
(Mean values for 5 l artificial serum)

Cation	Influent artificial serum	Effluent artificial serum			
		SR I	SR II	SR III	SR IV
Ammonium $\mu\text{g NH}_3\text{-N}\%$	100.0	20.0	22.0	18.5	20.0
Sodium meq/l	138.0	141.0	146.0	146.0	144.0
Potassium m q/l	4.1	5.0	2.4	2.6	2.4
Calcium meq/l	5.0	<u>2.2</u>	2.6	2.7	3.5
Magnesium meq/l	2.0	0.0	0.0	0.15	0.1

SR = Slurried Resin

It is seen that with all the four slurried resins about 80% of the ammonium is removed from the influent artificial serum: 3.0 to 8.0 meq/l increase in the sodium concentration was found with all the four. Potassium increased by 1.23 meq/l in the case of SRI, whereas it decreased by 1.44, 1.7 and 1.4 meq/l in the case of SR II, III and IV respectively. Calcium decreased by 2.8, 2.4, 2.3, and 1.5 meq/l in the case of SR I, II III and IV respectively, while magnesium was almost completely removed by all the four.

DISCUSSION

Quantitative studies on ammonium removal from the extra-corporeal circulation system have been reported on the basis of weight of the commercially bottled resins (4, 12, 13, 15, 17, 18, 19, 24, 25). These resins are usually moist, their water content may vary under different conditions of humidity and their exchange capacity may not be absolutely the same (Table I). Furthermore, fundamental studies on ion-exchange kinetics have always been made on the basis of ion-exchange capacity of the resins (21.) The quantity of the resin used for the present study, therefore, has been calculated with respect to its ion-exchange capacity expressed in milliequivalents.

Sodium form of the strong cation exchange resin, Amberlite IR-120, has been found to have maximum affinity for the divalent cations of the artificial serum (Table II). These results are in agreement with the fundamental exchange behaviour of this form of the resin (11, 22). Various other forms of the resin were found to be equally efficient in the ammonium removal but in each case there were marked cationic concentration changes (especially Ca^{++} and K^{+}) in the effluent artificial serum. Therefore, no single form of the resin was found to be suitable for the extracorporeal circulation system.

Development of a serious post-perfusion hypokalemia, hypocalcemia and hypomagnesemia has been reported by the use of the sodium form of the resin in the extracorporeal circuits (3, 17, 24, 25). These authors have tried to replace the loss of these cations by intravenous infusions of salts of potassium, calcium, and magnesium. However, in addition to increase in sodium, this would increase the total electrolyte concentration of blood, which may not be desirable. The ideal arrangement would be to prepare a suitable mixture of the four resin forms, which would remove excessive ammonium without any other change in the composition of blood.

The quantity of the various resin forms used (solid phase) and the volume and composition of the artificial serum (liquid phase) were kept constant at 75 meq and 5l respectively. Other experimental conditions viz. the particle size of the resin, temperature, flow rate, length and diameter of the resin columns, were also kept constant. It was therefore, possible to calculate approximately the comparative affinities of the various cations for the resin and they gave a much better picture of the relative changes in the cation concentration with different forms of the resin (Table III). On the basis of these calculations, a mixture (mixture 'B') of the four resin forms was worked out which was efficient in removing 48% of the ammonium from the artificial serum without any appreciable change in its other cations (Table V).

Ching and associates (3) attempted the use of a mixture of sodium and potassium forms of the strong cation exchange resin. The proportion of the potassium form of the resin in the mixture was 6% by weight. With this mixture they could adjust the potassium concentration of the effluents between 4 to 5.5 meq/l, which is almost a normal blood level. However, they did not try to find out the changes in the concentrations of other cations of the effluent blood. To have a clear idea of the efficacy and or defects of the mixture of sodium and potassium forms of the resin, an experiment was performed using a mixture (75 meq.) of sodium and potassium forms of Amberlite IR-120 resin, in which the potassium form of the resin was present to the extent of 6% in terms of exchange capacity. The results with the use of this mixture (Table VIII) showed an increase in the Na^+ concentration and a marked decrease in the Mg^{++} concentration of the effluent artificial serum; K^+ concentration remained unchanged while Ca^{++} was completely removed. Therefore, compared to the mixture of four resin forms (mixture 'B') of the present study, the mixture of two resin forms of Ching and associates (3) could not be satisfactorily employed in the extracorporeal circuits.

TABLE VIII: Effect of mixture of sodium (70.5 meq) and potassium (4.5 meq) forms of the resin on the uptake of ammonium and on other cations of the artificial serum. Flow rate, 60 ml/min.
(Mean values for 5 l artificial serum)

Artificial serum	Ammonium $\mu\text{g. NH}_3\text{-N}\%$	Sodium meq/l	Potassium meq/l	Calcium meq/l	Magnesium meq/l
Effluent	47	146	4.0	0.0	0.45
Influent	100	138	4.1	5.0	2.0

Increasing the quantity of the mixture 'B' resulted in increased uptake of ammonium and complete removal of ammonium was affected with 750 meq quantity of the mixture 'B' (Fig. 2). This increased ammonium uptake was found to be non-linear with the increase in quantity of the mixture 'B'. These results are in agreement with the fundamental exchange behaviour of this type of the resin (1, 11, 21, 22). However, increased quantities of the mixture 'B' (especially mixture B x 10,750 meq), were found to be accompanied by marked changes in the concentrations of other cations of the artificial serum, particularly Na^+ and K^+ . The resin mixture 'B' was worked out on the basis of affinities of various cations for the solid phase (75 meq) when 5 l, of the artificial serum (liquid phase) was passed through it under standardized conditions (Table III). These two phases, i.e. the solid phase and the liquid phase, are important variable factors and could give variable results when the quantity of either of the two is changed. It is important that one of these two factors should be kept constant and for this a 5 l, volume of the artificial serum was chosen corresponding to the approximate blood volume in humans. The proportion of various resin forms in the resin mixtures was altered, on the basis of their exchange behaviour (Table III), to work out suitable new resin mixtures. These resin mixtures (Table IV) have been found to be equally efficient in the ammonium removal compared to the various quantities of the mixture 'B' (Table V). The advantage with the new resin mixtures was that with their use no appreciable changes occurred in the other cations of the effluent artificial serum (Table V).

The absolute quantity of ammonium taken up by the resin mixture 'G' decreased with increased volume (from 5 l, to 10 l) of the influent artificial serum (Fig. 3). These results for the exhaustion studies are in agreement with those reported by Kissack *et al.* (15) for their slurried resins. The quantities of the various new resin mixtures have adjusted for the passage of 5 l, of the artificial serum only. Therefore, for any additional passage of the artificial serum (or blood), it is preferable to use fresh resin mixture columns in the ion-exchange circuits for optimum ammonium removal.

The slurry technique of Kissack *et al.* (15) has been re-evaluated in detail in the present study. From the results (Table VII) various slurried resins have been found to be equally efficient in the ammonium removal, but it was accompanied by marked changes in the concentrations of other cations, particularly Ca^{++} and Mg^{++} of the effluent artificial serum. Hence these mixed resin forms of Kissack *et al.*, (15) are not absolutely satisfactory for use in the extracorporeal circuits. They need suitable alterations in such a way that concentration of Na^+ , K^+ , Ca^{++} and Mg^{++} of the effluents are not significantly affected. To achieve this, these authors should have slurried the sodium form of the resin with a solution containing not only CaCl_2 and KCl but also containing some soluble salt of magnesium e.g. MgCl_2 . Furthermore, the concentrations of these salts in the slurry solution had to be adjusted by a systematic analysis of both influents and effluents for various cation. The present study with the mixtures of various resin forms on the other hand, is a systematic study as result of which the composition of various suitable resin mixtures has been worked out. Also, it is convenient to prepare various resin mixtures simply by mixing known quantities of the already prepared various forms i.e. sodium form, potassium form, calcium form and magnesium form of the strong cation exchange resin. Because of the optimum ammonium removal with its use, the resin mixture 'G' (750 meq), was considered to be the ideal resin mixture out of all the new mixtures studied (Table V).

Schechter *et al.* (24) after their experience with the sodium form of the resin, had mentioned that 'a device containing resin extracting mainly ammonium, would in this capacity, function as an "artificial liver". The resin mixture 'G' of the present study, therefore, could be described as an ammonium specific resin and could be safely employed in the extracorporeal circulation system for the removal of excessive ammonium. Furthermore, detailed *in vivo* studies, reported earlier (7, 8, 9, 10) had confirmed the efficacy of this mixture in the correction of experimental hyperammonemia in dogs unaccompanied by any harmful effects.

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