AN EXAMINATION OF RUBBER USED AS A CLOSURE FOR CONTAINERS OF INJECTABLE SOLUTIONS

PART III. THE EFFECT OF THE CHEMICAL COMPOSITION OF THE RUBBER MIX ON PHENOL AND CHLOROCRESOL ABSORPTION

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OWING to the variable composition of rubber it is possible that certain constituents in the mix may increase or decrease the absorption of phenol or chlorocresol. To determine whether this is so, several rubbers of known composition have been examined in which the fillers, accelerators and vulcanisers have been varied.

EXPERIMENTAL AND RESULTS

Effect of Fillers

Eight rubber mixes were prepared containing three fillers having the possibility of chemical interaction, namely zinc oxide, magnesium carbonate and calcium carbonate and four which exert a reinforcing action to the rubber matrix, namely china clay, VN3 (a precipitated silica), lampblack and philblack, the remaining mix containing the curing ingredients only. All the mixes were vulcanised in a press for 12 minutes at 60 lb. per square inch steam pressure (approx. 153° C.). The compositions are given in Table I.

TABLE I

COMPOSITION OF RUBBER SAMPLES 11–18

Sample number	11	12	13	14	15	16	17	18
Ingredient by weight—								
Smoked sheet rubber	100	100	100	100	100	100	100	100
Sulphur	2·5	2·5	2·5	2·5	2·5	2·5	2·5	2·5
Santocure	1·25	1·25	1·25	1·25	1·25	1·25	1·25	1·25
Zinc oxide	5	25	5	5	5	5	5	5
VN3-Silica	—	—	38	—	—	—	—	—
Calcium carbonate	—	—	—	52	—	—	—	—
Magnesium carbonate	—	—	—	—	44	—	—	—
Lampblack	—	—	—	—	—	36	—	—
Philblack	—	—	—	—	—	—	36	—
China clay	—	—	—	—	—	—	—	52

Santocure is *N-cyclo*hexyl-2-benzothiazol sulphenamide which splits at vulcanisation temperature into mercaptobenzothiazole and *cyclo*hexylamine.

Approximately 2 g. of each sample of rubber was placed in tubes containing 10 ml. of 0·5 per cent. phenol solution or 0·1 per cent. chlorocresol solution and the tubes sealed. The rubber in phenol solutions was stored for 14 days at 37° C. and that in chlorocresol solutions stored at 37° C. for 23 days in order to establish equilibrium between the rubber mix and the solution. All were then opened and determinations made of the phenol or chlorocresol content of the solutions. In all instances the partition coefficients were calculated for each sample (Table II).

TABLE II

PARTITION COEFFICIENTS FOR RUBBER SAMPLES 11–18

Sample number	Specific gravity of rubber	$K^{37^\circ C.}_{0.5}$ for phenol		$K^{37^\circ C.}_{0.1}$ for chlorocresol	
		Readings	Mean	Readings	Mean
11	0·935	0·87 0·84	0·86	15·5 14·9	15·2
12	1·068	0·89 0·82	0·86	14·3 14·7	14·5
13	1·055	1·21 1·17	1·19	22·8 24·1	23·4
14	1·172	0·91 0·93	0·92	17·3 17·3	17·3
15	1·118	0·84 0·83	0·84	12·6 12·6	12·6
16	1·058	0·78 0·80	0·79	16·6 17·3	17·0
17	1·027	0·85 0·87	0·86	17·8 17·5	17·6
18	1·162	0·98 0·78	0·89	15·0 14·9	15·0

It is seen that apart from the VN3—a precipitated silica—which results in a higher degree of absorption, the addition of the fillers mentioned do not influence the amount of absorption to any marked extent.

A further series of rubber mixes were prepared to show whether variation in the amount of filler had any effect on the phenol or chlorocresol absorption. One sample contained no filler, the others variable amounts of VN3, and calcium carbonate as shown in Table III.

TABLE III

COMPOSITION OF RUBBER SAMPLES 19–24 PREPARED BY VULCANISING AT 60 LB. PER SQUARE INCH STEAM PRESSURE (APPROX. 153° C.) FOR 12 MINUTES

Sample number	19	20	21	22	23	24
Pale crepe rubber ..	100	100	100	100	100	100
Zinc oxide	5·0	5·0	5·0	5·0	5·0	5·0
Sulphur	2·5	2·5	2·5	2·5	2·5	2·5
Santocure	1·25	1·25	1·25	1·25	1·25	1·25
VN3	—	10·0	40·0	—	—	—
Calcium carbonate ..	—	—	—	10·0	20·0	40·0

The rubber samples 19–24 were subjected to storage under the same conditions as samples 11–18, and the partition coefficients for each were calculated. These are shown in Table IV.

The results show that VN3 used as a filler increases phenol and chlorocresol absorption and is related to the amount of filler present. On the other hand calcium carbonate has little or no effect on this property even when the calcium carbonate content of the mix varies considerably.

The composition of rubber samples 25–34 is given in Table V.

Effect of the Variation in Sulphur Content

Four samples 25, 26, 27 and 19 differing only in the sulphur content were stored with phenol and chlorocresol solutions under the same

conditions mentioned above. The partition coefficients which are given in Table VI were calculated.

This shows that although the degree of absorption of chlorocresol rose slightly with an increase of the sulphur content of the mix, variation

TABLE IV

PARTITION COEFFICIENTS FOR RUBBER SAMPLES 19–24

Sample number	Specific gravity of rubber	$K_{0.5}^{37°\,C.}$ for phenol		$K_{0.1}^{37°\,C.}$ for chlorocresol	
		Readings	Mean	Readings	Mean
19	0·967	0·74 0·78	0·76	11·5 11·7	11·6
20	1·002	0·90 0·90	0·90	16·9 17·4	17·2
21	1·13	1·21 1·27	1·24	28·5 29·2	28·9
22	1·02	0·72 0·74	0·73	12·4 12·4	12·4
23	1·07	0·75 0·77	0·76	10·9 11·7	11·3
24	1·152	0·73 0·77	0·75	10·9 11·2	11·1

TABLE V

COMPOSITION OF RUBBER SAMPLES 25–34

Sample number	25	26	27	28	29	30	31	32	33	34
Ingredients by weight										
Pale crepe rubber ..	100	100	100	100	100	100	100	100	100	100
Zinc oxide	5·0	5·0	5·0	5·0	5·0	5·0	0·5	0·75	1·0	1·5
Santocure	1·25	1·25	1·25	—	—	—	—	—	—	—
Sulphur	1·0	1·5	2·0	1·5	1·5	1·5	1·5	1·5	1·5	1·5
P.T.D.	—	—	—	—	0·4	—	0·4	0·4	0·4	0·4
M.S.	—	—	—	0·4	—	—	—	—	—	—
M.B.T.S.	—	—	—	—	—	0·125	—	—	—	—
T.M.T.	—	—	—	—	—	0·25	—	—	—	—

P.T.D. = Dipentamethylenethiuram disulphide.
M.S. = Tetramethylthiuram monosulphide.
M.B.T.S. = Benzothiazyl disulphide which breaks down to mercaptobenzothiazole.
T.M.T. = Tetramethylthiuram disulphide.

Samples 28, 29 and 30 were cured for 6 minutes at 60 lb. per square inch steam pressure. Samples 25–27 and 31–34 were cured for 12 minutes at the same steam pressure.

TABLE VI

PARTITION COEFFICIENTS FOR RUBBER SAMPLES 19, 25, 26 AND 27

Sample number	Parts of sulphur	Specific gravity of rubber	$K_{0.5}^{37°\,C.}$ for phenol		$K_{0.1}^{37°\,C.}$ for chlorocresol	
			Readings	Mean	Readings	Mean
25	1·0	0·963	0·75	0·75	9·11 9·41	9·26
26	1·5	0·934	0·73 0·73	0·73	9·25 9·27	9·26
27	2·0	0·976	0·74 0·77	0·76	11·2 11·5	11·4
19	2·5	0·967	0·74 0·78	0·76	11·5 11·7	11·6

of the latter from 1 to 2·5 parts of sulphur had little influence upon the extent of phenol and chlorocresol absorption.

Effect of the Variation of Zinc Oxide Content

Samples 31, 32, 33, 34 and 29 containing between 0·5 and 5·0 parts of zinc oxide were stored with phenol and chlorocresol solutions under the same conditions mentioned above. The partition coefficients are given in Table VII.

TABLE VII

PARTITION COEFFICIENTS FOR RUBBER SAMPLES 31, 32, 33, 34 AND 29

Sample number	Parts of zinc oxide	Specific gravity of rubber	$K^{37^\circ C.}_{0.5}$ for phenol		$K^{37^\circ C.}_{0.1}$ for chlorocresol	
			Readings	Mean	Readings	Mean
31	0·5	0·933	0·94 0·88	0·91	18·5 18·7	18·6
32	0·75	0·931	0·88 0·91	0·89	18·2 18·4	18·3
33	1·0	0·936	0·88 0·87	0·88	18·2 17·8	18·1
34	1·5	0·938	0·85 0·87	0·86	18·2 17·8	18·0
29	5·0	0·966	0·82 0·87	0·85	17·6 17·4	17·5

The results show a very slight decrease in phenol and chlorocresol absorption with an increase in the zinc oxide content and such that a variation in the zinc oxide content can only be regarded as having no significant effect. A similar observation can be seen with samples 11 and 12 in which 5 and 25 parts of zinc oxide are present by weight and the accelerator used was Santocure.

TABLE VIII

PARTITION COEFFICIENTS FOR SAMPLES 26, 28, 29 AND 30

Sample number	Accelerator	Specific gravity of rubber	$K^{37^\circ C.}_{0.5}$ for phenol		$K^{37^\circ C.}_{0.1}$ for chlorocresol	
			Readings	Mean	Readings	Mean
26	Santocure	0·934	0·73 0·73	0·73	9·25 9·27	9·27
28	M.S.*	0·968	0·81 0·86	0·84	16·2 16·3	16·3
29	P.T.D.*	0·966	0·82 0·87	0·85	17·6 17·4	17·5
30	M.B.T.S.* T.M.T.	0·968	0·80 0·78	0·79	16·2 16·1	16·2

* See footnote to Table V for nomenclature.

Effect of the Use of Various Accelerators

Three rubber mixes were prepared containing as accelerators (1) dipentamethylenethiuram disulphide, (2) tetramethylthiuram monosulphide and (3) a mixture of benzothiazyl disulphide, which breaks down to mercaptobenzothiazole, and tetramethylthiuram disulphide. They were

cured for 6 minutes at 60 lb. per square inch steam pressure (approx. 153° C.).

The samples 28, 29 and 30, whose composition is given in Table V, were subject to storage in contact with phenol and chlorocresol solutions and the partition coefficients calculated. These are given in Table VIII and are compared also with sample 26 in which Santocure was used as accelerator but which was subject to 12 minutes curing at 60 lb. steam pressure.

There is little difference between the three mixes 28, 29 and 30 in phenol and chlorocresol absorption but they all show a higher absorption than the mix in which Santocure was used as the accelerator, although the curing time was twice as long for the latter.

Effect of a Plasticiser

A rubber mix of the same composition as sample 11 to which had been added 20 parts by weight of factice (an oxidation product of linseed oil), gave partition coefficients $K_{0\cdot5}^{37°\,C.}$ for phenol of 1·66 and $K_{0\cdot5}^{37°\,C.}$ for chlorocresol of 28·4. These results, confirmed by others where factice was a constituent, have shown that the presence of this substance causes a marked increase in phenol and chlorocresol absorption.

Discussion

The absorption of phenol and chlorocresol by rubber is unaffected to a large degree by the variation of the chemical composition of the mix. By comparing samples 11 and 12 where the relative sulphur and zinc oxide content varies considerably and yet the absorption remains practically constant, it can be seen that the difference between series 25–27 and 19, in which the sulphur content varies and series 31–34 and 29, in which the zinc oxide content varies, is obviously due to the accelerators Santocure and dipentamethylenethiuram disulphide which were used respectively rather than to varying sulphur and zinc oxide contents. Again, by reference to samples 25–34, in which 4 different accelerators were used and the curing time varied from 6 to 12 minutes, it is seen that although an increase in zinc oxide resulted in a slightly lower absorption, the more important difference was the lower absorption resulting from using Santocure when compared with the other acclerators rather than in the length of time of the cure.

The use of the plasticiser factice causes a marked increase in absorption by the rubber as also did the filler VN3. Of all other substances used none seemed to affect the absorption markedly, but it is important to note than by comparing samples 11 and 19 which differed only in the rubber employed in the mix, that absorption variation may also arise from the type of crude rubber used in the mix.

Summary

1. Rubbers of simple composition have been examined to determine whether variation of composition of the main types of ingredient cause any variation in the absorption of phenol or chlorocresol.

2. Rubber containing the fillers zinc oxide, calcium carbonate, magnesium carbonate, lampblack, philblack and china clay shows little variation from rubber containing no filler in their phenol and chlorocresol absorption.

3. The presence of VN3—a precipitated silica, results in an increased absorption which is related to the VN3 content.

4. An increase in sulphur content results in a slightly higher absorption.

5. An increase in zinc oxide content results in a slightly decreased absorption.

6. The accelerator Santocure (*N-cyclo*hexyl-2-benzothiazol sulphenamide) produces a rubber having a lower degree of absorption than when dipentamethylenethiuram disulphide, tetramethylthiuram monosulphide, benzothiazyl disulphide, and tetramethylthiuram disulphide are used. These latter produce rubbers with a similar degree of absorption.

7. The inclusion of factice as a plasticiser causes a marked increase in the absorption.

8. Variation in the natural rubber used can result in a difference in the amount absorbed by the cured rubber mix.

In conclusion I wish to thank Messrs. J. C. Franklin & Son and particularly Dr. R. H. Muller for preparing and making available the special rubber mixes used in this investigation, also Dr. B. E. Tomlinson and Mr. G. B. Pendleton for the use of certain equipment.

DISCUSSION

The papers were presented by the AUTHOR.

DR. G. E. FOSTER (Dartford) asked for more information about the physical condition of the samples of rubber used.

MR. R. L. STEPHENS (Brighton) said that the time of vulcanisation was important. Had the author determined the equilibrium constants using the same mix of rubber which had been given different vulcanising times?

MR. F. G. FARRELL (London) said the rate of absorption was also a function of the surface area of the rubber exposed to the solution and he asked the author to give the diameter and thickness of the rubber tubing used.

MR. D. H. MADDOCK (Dagenham) said that it had been reported that silicone plugs were very satisfactory for multidose containers. Had the author carried out any work with them?

MR. G. R. WILKINSON (London) asked whether the author had any information on the physical properties and suitability for use of the rubber after exposure to the chlorocresol.

DR. J. C. PARKINSON (Brighton) said it would be interesting to know if caps stored for 28 days until equilibrium was reached and then dried, absorbed more chlorocresol when they were used.

MR. T. D. WHITTET (London) asked if the other physical properties of the various samples of rubber tested had been examined.

MR. W. P. HUTCHINSON (Oxford) said it would be of interest to determine whether irradiation of rubber would render the surface impervious to chlorocresol.

MR. W. T. WING, in reply, said that the samples which he handled were cut from sheets approximately $\frac{1}{16}$ in. thick. The pieces were $\frac{1}{4}$ in. wide and 5 cm. long; this gave approximately 2 g. in each case. The rubbers prepared for his work were subjected to different heating times. In one case it was six minutes at 60 lb. pressure and in another twelve minutes, and in comparing the two there was little difference in the amount of absorption. Silicone caps were entirely unsatisfactory in that they were not sufficiently elastic and were not self-closing. He had investigated the physical properties of the rubbers which he had examined but had published no details. His main concern had been to examine chlorocresol and phenol absorption to try and find out the factors which affected it.