Irritant Action of Binary Soap Mixtures on Skin[1]*

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Introduction

IN previous work (1) values for the irritant action of soaps made from the chemically pure, single fatty acids were obtained as follows: (Male skin—percent positive reactions using sodium soaps) caprylic acid 0.0%, capric acid 8.3%, lauric 70.7%, myristic acid 29.1%, palmitic acid 0.0%, stearic acid 0.0%, oleic acid 12.5%, linoleic acid 8.3% and ricinoleic acid 8.3%. Similar tests on female skin gave generally higher percent positive reactions: caprylic acid 7.1%, capric acid 42.8%, lauric acid 85.7%, myristic acid 64.2%, palmitic acid 14.3%, stearic acid 0.0%, oleic acid 28.5%, linoleic acid 64.2% and ricinoleic acid 28.5%.

Since sodium salts of inorganic acids enhance the irritant action of soaps (2), and since commercial soaps represent complex mixtures of the salts of various fatty acids, it appeared logical to investigate the possibility of one fatty acid salt augmenting or inhibiting the irritant action of another fatty acid salt.

Method Used

Such binary mixtures were tested for their irritant action on human skin according to the following method: A square rubber mat with a circular hole in the center designed to hold a Koromex rubber diaphragm, size 50, and with adjustable elastic bands to hold the apparatus around the arm or leg was prepared. The diaphragm, charged with 15 c.c. of a soap mixture and with the application of a small amount of tragacanth jelly on the rim to ensure against leakage, was then fitted into the circular aperture of the mat. In turn, the whole preparation was secured to the inner surface of the arm or leg by means of the elastic bands. Time of contact of the soap mixtures with the skin in all tests was four hours. Excepting a small margin where the rim of the diaphragm pressed against the skin any manifestation of irritation was assumed to be due to the irritant action of the soap mixture. In interpreting the results of the patch tests, subjects were scored ++ if the whole area covered by the soap mixture in the diaphragm was reddened or if the diaphragm had to be removed before the end of the four-hour period because of pain. Small patches of redness were scored as +, faint erythema was marked ±, and failure to show any reaction was rated as —. In calculating the percent of positive reactions, all degrees of positive reactions were counted as positive.

Binary Mixtures

The final concentration of all soap mixtures, as in previous work, was 0.0225 N. To obtain a binary mixture with this final concentration 2/3 of the amount of one soap necessary to make a 0.0225 N solution plus 1/3 of the amount of a second soap required to effect a mixture of the same concentration were added to the calculated amount of water. Thus, in the sodium laurate-sodium caprylate mixture the same molecular concentration as in a 0.0225 N sodium laurate solution was obtained, but 2/3 of those molecules were C_{12} and 1/3 were C_8. It was assumed that the C_{12} molecules would produce 2/3 of the irritant action as observed for a 0.0225 N sodium laurate solution, and the C_8 molecules would produce 1/3 of the irritant action as noted for a 0.0225 N sodium caprylate solution. The sum of these two values was taken as the expected percent positive irritation for this binary mixture of sodium laurate and sodium caprylate. For example: sodium caprylate on females gave 7.1% positive reactions and sodium laurate on females gave 85.7% positive reactions; thus, $(2/3 \times 85.7) + (1/3 \times 7.1) = 59.5\%$ positive reactions to be expected on females with the laurate-caprylate mixture.

Since sodium laurate of the soaps at hand was known to be possessed of the greatest irritating power, it was chosen to constitute the major portion of the binary mixture of the first series tested—for results see Table I. The results of the first series of tests indicated, on male skin at least, that laurates were inhibited by oleates; therefore, the binary mixtures of the second series, using this lead, were composed of one part oleate and two parts of another soap—see Table II. The results of the first series further indicate that a laurate soap was augmented by a caprylate soap; thus, in the third series of binary mixtures one part of sodium caprylate was combined with two parts of some other sodium soap—see Table III.

Results of Tests of Binary Mixtures on Human Skin

The obtained results for the three series of binary mixtures are given in Tables I, II, and III.

Discussion of Results

It is difficult to analyze the results obtained. Skin is not a standardized structure. The skin of individuals of the same sex and age show a marked variation of response to the same soap, and this, of course, is a source of error. The only way this error can be minimized is to perform thousands of tests for each mixture. Certainly, small differences between the calculated percent positive reactions and the obtained percent positive reactions in the above results cannot be regarded as significant. The variation of responses of skins to a given concentration of a soap suggests that a soap enters different skins at different rates and that after entrance a minimal threshold amount of the soap is necessary to irritate. Any amount of the soap in excess of this minimal threshold amount would, no doubt, produce a greater irritant action, but the increment of increase of the irritant action would probably be greatest where the soap concentration is the closest to the minimal threshold amount. Determination of such different

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TABLE I.

Results of the Binary Mixture of 0.0150 N. Sodium Laurate and 0.0075 N. Indicated Soap.

Indicated soap	Appearance	Ph @ 24°C.	♀ Positive reactions	♀ Negative reactions	♀ Percent positive	♀ Calculated positive	♀ Difference	♂ Positive reactions	♂ Negative reactions	♂ Percent positive	♂ Calculated positive	♂ Difference
Sodium caprylate	Clear	8.52	37	3	92.5	59.5	+ 33.0	16	7	69.6	47.1	+ 22.5
Sodium caprate	Clear	8.41	14	6	70.0	73.7	− 3.7	11	12	47.8	49.9	− 2.1
Sodium laurate	Clear	8.70	12	2	85.7	85.7	.....	17	7	70.7	70.7	.....
Sodium myristate	White suspension	9.87	12	8	60.0	78.5	− 18.5	9	14	39.1	56.8	− 17.7
Sodium palmitate	White gel	9.83	14	7	66.6	61.9	+ 4.7	10	13	43.5	47.1	− 3.6
Sodium stearate	White gel	9.73	16	4	80.0	57.1	+ 22.9	8	15	34.8	47.1	− 12.3
Sodium oleate	Slightly turbid	8.79	30	9	76.9	66.6	+ 10.3	3	20	13.0	51.3	− 38.3
Sodium ricinoleate	Clear	9.11	15	5	75.0	66.6	+ 8.4	10	13	43.5	49.9	− 6.4
Sodium linoleate	Clear	8.45	11	9	55.0	78.5	− 23.5	8	15	34.8	49.9	− 15.1

♀ = Female skin.

♂ = Male skin.

rates of entrance and minimal irritation threshold values were not attempted in this paper.

The results in Table I, excluding small differences between obtained and calculated percent positives, indicate that on female skin the irritant action of sodium laurate is augmented by sodium caprylate and sodium stearate, and is inhibited by sodium linoleate. On male skin, there is, again, an augmentation in the case of sodium caprylate and an inhibition by sodium oleate. Neither the physical properties of the mixtures nor the hydrogen ion concentrations offer any clew as to an explanation for these results. Since sodium chloride and sodium carbonate added to sodium alkyl sulfates enhance irritation, it may be argued that sodium caprylate added to sodium laurate acts in a similar way, but then sodium caprate would be expected to show a value close to that of caprylate.

In the first series, sodium oleate appeared to inhibit the irritant action of sodium laurate on male skin. The second series, therefore, was set up to determine if sodium oleate would depress the irritant action of all the test soaps. The results obtained do not bear out this point. In fact, on both female and male skins the ricinoleate mixture shows considerable toxicity. Likewise, the caprate, the myristate, the palmitate, and the stearate mixtures give augmentations on female skin. The linoleate mixture in the case of female skin exhibits a definite reduction of activity. Here again no plausible explanation is at hand. There is the possibility that in the first series the amount of sodium laurate used was below the effective amount for male skin, and even with the additive effect of another soap, the total irritation was not sufficient to be scored as positive. Again, pH and physical properties are of little help.

The noted enhancement of the irritant action of sodium laurate by sodium caprylate in Table I is the basis for the third series as seen in Table III. In a

TABLE II.

Results of the Binary Mixture of 0.0075 N. Sodium Oleate and 0.0150 N. Indicated Soap.

Indicated soap	Appearance	Ph @ 24°C.	♀ Positive reactions	♀ Negative reactions	♀ Percent positive	♀ Calculated positive	♀ Difference	♂ Positive reactions	♂ Negative reactions	♂ Percent positive	♂ Calculated positive	♂ Difference
Sodium caprylate	Slightly turbid	7.94	7	14	33.3	14.2	+ 19.1	2	18	10.0	4.2	+ 5.8
Sodium caprate	Slightly turbid	7.83	13	7	65.0	38.0	+ 27.0	3	17	15.0	9.7	+ 5.3
Sodium laurate	Slightly turbid	8.79	30	9	76.9	66.6	+ 10.3	3	20	13.0	51.3	− 38.3
Sodium myristate	White suspension	9.63	16	3	84.2	52.3	+ 31.9	3	18	14.3	23.6	− 9.3
Sodium palmitate	White gel	10.11	9	8	52.9	19.0	+ 33.9	4	17	19.0	4.2	+ 14.8
Sodium stearate	White gel	10.15	6	14	30.0	9.5	+ 20.5	1	20	4.8	4.2	+ 0.6
Sodium ricinoleate	Clear	8.67	14	6	70.0	28.5	+ 41.5	7	14	33.3	9.7	+ 23.6
Sodium linoleate	Slightly turbid	7.60	5	15	25.0	52.3	− 27.3	2	19	9.5	9.7	− 0.2
Sodium oleate	Clear	10.0[illegible]	4	10	28.5	28.5	.....	3	21	12.5	12.5	.....

♀ = Female skin.

♂ = Male skin.

TABLE III.

Results of the Binary Mixture of 0.0075 N. Sodium Caprylate and 0.0150 N. Indicated Soap

Indicated soap	Appearance	Ph @ 24°C.	♀ Positive reactions	♀ Negative reactions	♀ Percent positive	♀ Calculated positive	♀ Difference	♂ Positive reactions	♂ Negative reactions	♂ Percent positive	♂ Calculated positive	♂ Difference
Sodium caprate	Clear	7.23	1	8	11.1	30.9	−19.8	2	9	18.2	5.5	+12.7
Sodium laurate	Clear	8.52	37	3	92.5	59.5	+33.0	16	7	69.6	47.1	+22.5
Sodium myristate	White gel	10.02	7	3	70.0	45.2	+24.8	0	11	0.0	19.4	−19.4
Sodium palmitate	White gel	10.05	2	8	25.0	11.9	+13.1	1	9	10.0	0.0	+10.0
Sodium stearate	White gel	9.95	0	10	0.0	2.4	−2.4	1	11	8.3	0.0	+8.3
Sodium ricinoleate	Clear	9.06	4	3	57.1	21.2	+35.9	2	5	28.6	5.5	+23.1
Sodium linoleate	Slightly turbid	7.30	1	9	10.0	45.2	−35.2	1	7	12.5	5.5	+7.0
Sodium caprylate	Clear	7.10	1	13	7.1	7.1	.....	0	24	0.0	0.0	.....
Sodium oleate	Slightly turbid	8.02	3	5	37.5	21.4	+16.1	1	7	12.5	8.3	+4.2

♀ = Female skin.

♂ = Male skin.

general way sodium caprylate appears to give an augmentation of irritant action especially in the cases of sodium laurate, sodium myristate, and sodium ricinoleate on both female and male skins. The exceptions to this generalization are sodium caprate, sodium stearate, and sodium linoleate on female skin, and sodium myristate on male skin.

For a soap to cause irritation of human skin certain requirements must be met. One essential requirement appears to be the entrance of the soap into the layers of the skin, and since it is generally recognized that non-ionized or undecomposed soap has the greatest wetting power, it seems logical that soap to a large degree enters the layers of the skin in the undecomposed form. The size of the molecule, solubility, colloidal nature, etc., would of course have a bearing on the ease of entrance. After the soap has entered the skin, it must reach a certain concentration before it can do harm. This would be the threshold level, and it may vary per soap and per skin. The higher the threshold level, the lower is the toxicity of the soap. This toxicity appears to be related to the fatty acid chain of the soap molecule and not necessarily to the sodium alone—if sodium alone were concerned sodium caprylate should be more irritant than sodium laurate. The exact mechanism of this toxic reaction is unknown. It has been demonstrated, however, that calcium deficits lead to intense stimulations of muscle and nerve tissues which might, in turn, produce injury and inflammation. This early irritation (itching, pain, erythemia) could be followed by a more severe toxicity caused by actual modifications of the cell proteins by the absorbed soaps. The threshold levels for the straight chain, saturated soaps, from hemolytic and earthworm experiments, seem, in general, to decrease (toxicity increase) as the series is ascended and to reach the lowest value with C_{12} to give laurates the greatest toxicity. Beyond laurates the insolubility, the increased size of the molecule, etc. (entrance into skin layers is impeded), come into predominance to lower the toxicity curve, otherwise, the toxicity curve might continue upwards from laurates as a straight line.

With this as a working hypothesis, the increase in irritation by a sodium soap in the presence of inorganic sodium salts could be explained on the basis that the ionization of the inorganic sodium salt reduces the ionization of the soap to increase the amount of undecomposed soap present. The enhancement of the irritant action of laurates by the presence of caprylates could be accounted for in the same manner. The decrease of irritant action by soaps on skins which have previously been subjected to alcohol baths according to this theory is to be expected on the grounds that the astringent action of the alcohol does not permit the entrance of the soap. Similarly, cleansers after soaps would aid in the removal of soaps from the skin. The irregularities noted when applying this idea of soap irritation to the results reported would be due to insufficient tests.

Conclusions

Evidence is offered in support of the following: (1) sodium laurate-sodium caprylate mixtures appear to be highly irritant to the skin of both sexes, (2) sodium ricinoleate binary mixtures with sodium laurate, sodium caprylate, and sodium oleate show a definite irritant action on human skin, (3) sodium linoleate binary mixtures with sodium laurate, sodium caprylate, and sodium oleate indicate a decreased irritant action, (4) sodium laurate-sodium myristate binary mixtures tend to be much less irritant to skin than can be predicted from their respective irritant powers.

REFERENCES

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