TABLE II

Preparation of Hydrazides from Methyl Esters

Ester	Yield 1st Cryst.	Yield 2nd Cryst.	Vol. 70% EtOH	M.P. Found (Cor.)	M.P. Lit.	N, Calcd.	N,* Found
	%	%	*ml.*				
C-10, Sebacate	91	85	60	188	188(4)	24.33	24.48
C-9, Azelate	95	89	60	187	.....	25.91	25.79
C-8, Suberate	85	68	50	187	187(8)	27.70	27.62
C-7, Pimelate	89	78	40	185	182(6)	29.77	29.67
C-6, Adipate	93	73	30	182	178(6)	32.16	31.90
C-5, Glutarate	97	68	30	176	176(5)	34.98	35.01
C-18, Stearate	.....	.....	.....	117	116(1)	.....	.....

* By the Pregl Micro Dumas Method.

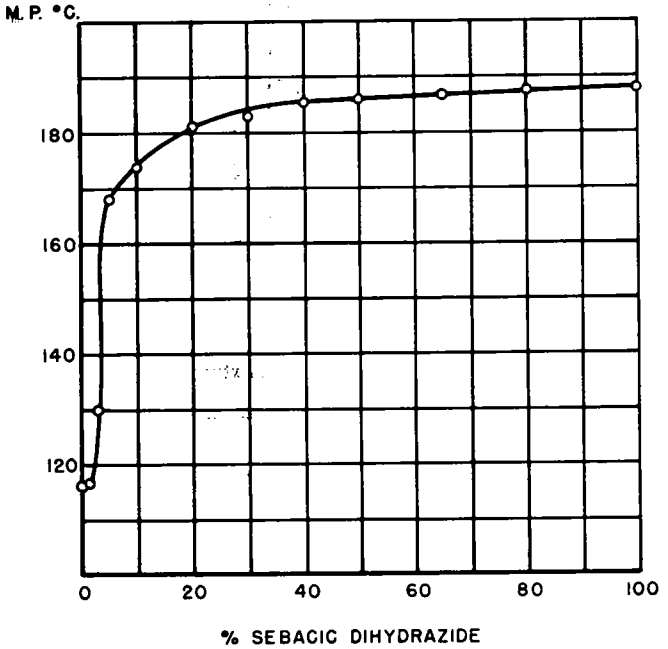

FIG. 2. Melting points of binary mixtures of stearic hydrazide and sebacic dihydrazide.

The binary mixture of stearic acid hydrazide and sebacic acid dihydrazide showed no eutectic formation by the method used. More refined methods might show a eutectic below 1-2% sebacic acid dihydrazide. The dihydrazide is very insoluble in the liquid hydrazide. Although the melting points differ by more than 70°, 50% of the stearic hydrazide lowered the melting point of the dihydrazide by only 1.5°, 35% by only 0.5°. It is obvious therefore that melting points may be of little value in determining purity of dihydrazides if some fatty acid monohydrazides are present and that melting points should always be supported by nitrogen determinations.

Summary

1. A simple preparation of the dihydrazides is given. The recrystallized dihydrazides of glutaric, adipic, pimelic, suberic, azelaic, and sebacic acids melted at 176, 182, 185, 187, and 188°C., respectively.

2. The melting point curves are reported for binary mixtures of a) the dihydrazides of adjacent members of the homologous series of dicarboxylic acids from glutaric to sebacic, b) suberic and sebacic dihydrazide, and c) sebacic dihydrazide and stearic hydrazide.

3. The binary mixtures of the dihydrazides show formation of a eutectic containing 52-53 weight per cent of the lower component.

4. The binary mixture of stearic hydrazide and sebacic dihydrazide shows no eutectic by the method used.

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Antioxidant Properties of Polyhydroxybenzoic Acids and Their Esters, and Other Nuclear Substituted Polyphenols*

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SINCE the original work of Moureu and Dufraisse (1) in 1922, in which they found that certain phenols had antioxygenic properties, many compounds have been studied as antioxidants in fatty materials. The phenols and compounds with phenolic functional groups, however, have remained one of the most important class of compounds as antioxidants for fats and oils. In 1933 Newton and Grettie obtained a United States patent (2) on the use of gum guaiac as an antioxidant. Gum guaiac is a secretion of a tropical tree, *Guaiacum officinale*, which grows in the West Indies. Its active principle is presumably guaiaretic acid, which is phenolic.

Gum guaiac was the first material to be approved for use in lard by the Meat Inspection Division of the Bureau of Animal Industry. This was in 1940. Later, nordihydroguaiaretic acid (NDGA), first re-

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ported by Lundberg, Halvorson, and Burr (3), also appeared on the approved list.

In 1941, a United States patent was issued to Sabalitschka and Boehm (4) covering other phenolic compounds for use as antioxidants, namely, the lower alkyl esters of gallic acid. The antioxidant properties of propyl gallate were described by Boehm and Williams (5) in 1943.

All the simple phenols have been tested as antioxidants, but no extensive work has been done on the derivatives of phenols. As early as 1931 Mattill (6), in a study of the hydroxy benzenes, concluded that the antioxygenic capacity of phenols resides in two hydroxyl groups in the ortho or para configuration; when these are in the meta position the compound is inactive. Olcott (7) found that a number of the polyhydroxy benzenes were excellent antioxidants for lard. The hexahydroxy benzene, however, had no antioxidant activity in spite of the fact that it was readily oxidized. Golumbic (8) showed that the stabilizing action of hydroquinone was finally lost with progressive nuclear methylation. The activity of the dimethyl hydroquinones varied with the positions of the methyl groups, and the trimethyl and tetramethyl hydroquinones were inactive.

The present paper reports a comparative evaluation of the antioxidant properties of several of the polyphenols in which various nuclear substitutions have been made.

Experimental

The substrate used in testing the antioxidants was a good-quality, steam-rendered lard.

Stability tests: The modification of the active oxygen method (A.O.M.) previously described (9) was employed for evaluating the antioxidants in the lard substrates. The antioxidants soluble in lard were incorporated into the lard by stirring and warming it gently on the steam bath. The insoluble antioxidants were incorporated by means of alcoholic solutions, and the solvent was removed in a laboratory deodorizer at 60°C., as described in a previous paper (10).

Baking tests: The baking tests were made on crackers. The cracker recipe consisted of a sponge mix and a dough mix. The sponge mix was made as follows: To 30 cc. of water were added 0.2 g. of dry yeast and 0.1 g. of sugar. The water solution was then added to 60 g. of cake flour in a glass bowl. This was mixed by hand with a porcelain spatula. The bowl was tightly covered and the contents were allowed to ferment for 19 hours in an incubator at 30°C.(86°F.).

After 19 hours the dough mix—consisting of 40 g. of dough flour, 11 g. of lard, 1 g. of salt, and 0.5 g. of baking soda dissolved in 3 cc. of water—was thoroughly mixed and then incorporated into the sponge by working them together by hand. The mixture was allowed to ferment for 5 hours at 30°C. The dough was then rolled into sheets about $\frac{3}{32}$ inch thick by a mechanical sheeter and cut into wafers 1 inch in diameter by an aluminum cutter. The wafers were docked with a glass or wooden pin and baked at 232°C.(450°F.) until slightly brown—8 to 9 minutes. (It is better to bake the various batches of crackers to a definite degree of browness as judged by the eye than to keep the baking time constant. A more uniform degree of baking can be obtained.) The crackers were allowed to stand overnight in the open air. They were then crisped for 7 minutes in the oven at 149°C.(300°F.).

The wafers were placed in 6-oz. wide-mouth bottles, covered with small watch glasses, and stored at 63°C. Rancidity was determined organoleptically.

TABLE I

Evaluation of Trihydroxybenzoic Acids and Their Esters as Antioxidants in Lard by the Active Oxygen Method

Antioxidant	Stability	
	0.005%	0.02%
	hours	*hours*
3,4,5-Trihydroxybenzoic acid (gallic)	40	105
2,3,4-Trihydroxybenzoic acid (pyrogallol o-carboxylic)	26	64
Dodecyl 3,4,5-trihydroxybenzoate	33	70
Dodecyl 2,3,4-trihydroxybenzoate	14	25
Control, 8½ hours		

Results and Discussion

Table I shows the comparative stabilizing action of gallic acid (3,4,5-trihydroxybenzoic acid) and pyrogallol o-carboxylic acid (2,3,4-trihydroxybenzoic acid) and their dodecyl esters. The gallic acid compounds were one and one-half to two times as active as the pyrogallol carboxylic acid compounds, as determined by A.O.M. tests. The apparent superiority of the acids over the esters, when compared on a weight basis, is due to the higher molecular concentration of the acids, the molecular weight of the acids being approximately one-half that of the esters.

TABLE II

Comparative Evaluation of Dihydroxybenzenes With Molecular Equivalent Amounts of the Dihydroxybenzoic Acids and Their Esters as Antioxidants in Lard

Antioxidants	A.O.M. Stability
	hours
None	8
0.0050% Catechol	32
0.0070% 3,4-Dihydroxybenzoic acid	13
0.0121% Octyl 3,4-dihydroxybenzoate	15
0.0147% Dodecyl 3,4-dihydroxybenzoate	15
0.0159% Tetradecyl 3,4-dihydroxybenzoate	12
0.0172% Hexadecyl 3,4-dihydroxybenzoate	14
0.0050% Hydroquinone	34
0.0070% 2,5-Dihydroxybenzoic acid	21
0.0121% Octyl 2,5-dihydroxybenzoate	12
0.0159% Tetradecyl 2,5-dihydroxybenzoate	12
0.0172% Hexadecyl 2,5-dihydroxybenzoate	11
0.0185% Octadecyl 2,5-dihydroxybenzoate	11
0.0050% Resorcinol	9
0.0070% β-Resorcylic acid	7
0.0070% α-Resorcylic acid	7½
0.0147% Dodecyl α-resorcylate	8

Table II gives a comparison of the antioxidant properties of some of the dihydroxybenzoic acids and esters with those of the corresponding parent phenols. The percentages of acids and esters used are equal in molecular amounts to that of 0.005% concentration of the parent phenols. Those dihydroxybenzoic acid series which may be considered as derivatives of catechol and of hydroquinone showed the highest antioxidant activity among the acids. Catechol and hydroquinone, however, were more than twice as active as the corresponding acids.

In Table III the stabilizing action of the esters of 3,4-dihydroxybenzoic acid and the esters of 2,5-dihydroxybenzoic acid are compared with NDGA and lauryl gallate. The results show that the dihydroxybenzoates are definitely inferior to the NDGA and lauryl gallate.

In Table IV antioxidant values of polyphenols are compared with those of equimolecular amounts of

TABLE III

Stabilizing Values of Different Amounts of Antioxidants in Lard

Antioxidant	A.O.M. Stability		
	0.05%	0.02%	0.01%
	hours	*hours*	*hours*
NDGA	81	114	106
Lauryl gallate	103	70	45
Octyl 3,4-dihydroxybenzoate	25	19	13
Dodecyl 3,4-dihydroxybenzoate	23	17	13
Tetradecyl 3,4-dihydroxybenzoate	24	16	12
Octadecyl 3,4-dihydroxybenzoate	24	17	12
Octyl 2,5-dihydroxybenzoate	14	....	11
Dodecyl 2,5-dihydroxybenzoate	15	....	....
Hexadecyl 2,5-dihydroxybenzoate	13	11	....
Octadecyl 2,5-dihydroxybenzoate	13	11	....
Control, 7 hours			

their derivatives. Inspection of the table reveals that the introduction of an acyl group into the nucleous of a polyphenol lowers the antioxidant activity, as measured by the active oxygen method. This seems to hold whether the acyl group is an acetyl group or larger, such as octoyl, dodecoyl, of octadecoyl group. Catechol, hydroquinone, and pyrogallol, each at 0.005% concentration in lard, have stabilities of

TABLE IV

Comparative Evaluation of Polyphenols and Molecular Equivalent Amounts of Their Derivatives

Antioxidants	A.O.M. Stability
	hours
None (control; prime steam lard)	8
0.0050% Catechol	32
0.0069% 4-Acetyl catechol	12
0.0095% 4-Hexoyl catechol	18
0.0088% 4-Hexyl catechol	67
0.0107% 4-Octoyl catechol	9
0.0101% 4-Octyl catechol	68
0.0133% 4-Dodecoyl catechol	17
0.0127% 4-Dodecyl catechol	40
0.0127% 3-Dodecyl catechol	66
0.0146% 4-Tetradecoyl catechol	16
0.0146% 3-Tetradecoyl catechol	11
0.0171% 4-Octadecoyl catechol	16
0.005% 4-Tert. butyl catechol	73
0.0050% Hydroquinone	34
0.0069% Acetyl hydroquinone	8
0.0050% Resorcinol	9
0.0050% Pyrogallol	87
0.0067% Acetyl pyrogallol	15

32, 34, and 87 hours, respectively. The stabilities of the acetyl derivatives of these same phenols, namely, acetyl catechol, acetyl hydroquinone, and acetyl pyrogallol are only 12, 8, and 15, respectively. Octoyl catechol, dodecoyl catechol, and tetradecoyl catechol have stabilities respectively of 9, 17, 16, as compared with 32 for catechol. By referring to Table II, it is seen that the introduction of a carboxyl into the nucleus also lowers the antioxidant activity of the phenol. This holds true for the esterified carboxyl as well as for the free carboxyl. However, the data in Table IV indicate that when an alkyl group is substituted into the nucleus the antioxidant activity of the phenol is enhanced. When hexoyl, octoyl, and dodecoyl catechol derivatives were reduced by hydrogenation to form 4-hexyl, 4-octyl, and 4-dodecyl catechols, the alkyl catechols had stabilities of 67, 68, and 40. 3-Dodecyl catechol and 4-tertiary butyl catechol showed stabilities of 66 and 73.

It should be emphasized at this point that these generalizations regarding nuclear substitution of phenols and their stabilizing effect apply only to the stability as measured by A.O.M. That the generalizations do not hold for data obtained in baking tests with crackers is shown by Table V. Here the unsubstituted phenols show no carry-over into the baked crackers. The substituted phenols such as the gallate esters and the esters of 2,3,4-trihydroxybenzoic acid do show a small amount of carry-over. None of the compounds listed have good carry-over into baked crackers. The alkyl catechols show the most activity.

Summary and Conclusions

A study has been made of the antioxidant properties of a number of polyhydroxybenzoic acids and the higher alkyl esters of these acids, and also of the acyl and alkyl substituted polyphenols. The active oxygen method (A.O.M.) and baked cracker tests were used. In the A.O.M. tests the classes of compounds had the following ascending order of activity; acyl phenols, polyhydroxy benzoic acid esters, phenols, and several alkyl catechols. In the cracker tests the free phenols, acyl phenols, and dihydroxybenzoic acid esters showed little or no carry-over. The gallic acid (3,4,5-trihydroxybenzoic acid) esters and 2,3,4-trihydroxybenzoic acid esters showed a small amount of carry-over.

The alkyl catechols had the most activity of all the catechol derivatives in the A.O.M. and cracker tests.

TABLE V

Storage Life at 63°C. of Crackers Containing Various Amounts of Antioxidants

Antioxidant	Keeping time
	days
None (control; prime steam lard)	2
0.02% NDGA	2
0.05% NDGA	1
0.02% Gallic acid	2
0.05% Propyl gallate	3
0.02% Octyl gallate	1
0.05% Octyl gallate	3
0.02% Dodecyl gallate	1
0.05% Dodecyl gallate	4
0.02% Octadecyl gallate	3
0.05% Octadecyl gallate	4
0.01% Octadecyl 2,3,4-trihydroxybenzoate	4
0.02% Octadecyl 2,3,4-trihydroxybenzoate	4
0.05% Octadecyl 2,3,4-trihydroxybenzoate	4
0.01% Pyrogallol	2
0.02% 4-Hydroxybenzoic acid	2
0.025% 4-Dodecyl catechol	12
0.012% 4-Dodecyl catechol	11
0.015% Dodecyl 2,5-dihydroxybenzoate	3
0.015% Dodecyl 3,4-dihydroxybenzoate	2

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