Antioxidant Solubility and Efficiency

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Abstract □ The solubilities of a series of gallates in water, cetomacrogol solution, and benzaldehyde were determined at 25°. Methyl, ethyl, and propyl gallates were fairly water-soluble but octyl, decyl, and dodecyl gallates were practically insoluble. Generally, solubilities in water and in surfactant solutions increased with decrease in alkyl-chain length. The solubilities of the short-chain gallates in benzaldehyde increased while that of the long-chain members decreased with chain length. The comparative antioxidant efficiency in solubilized systems appeared to be related to the distribution ratios while that in emulsified systems to the solubility of the antioxidant in the aldehyde.

Keyphrases □ Antioxidants—gallates □ Gallates, solubility—cetomacrogol solution, water, benzaldehyde □ Solubility relation—antioxidant activity

Rosenwald *et al.* (1) measured the antioxidant efficiency of alkylated phenols by determining the amount of antioxidant concentration which allowed a standard amount of oxygen uptake during a fixed time interval. Under such conditions it was shown that the efficiency for an antioxidant per unit concentration was generally dependent on the concentration itself. In a later study, (2) the inhibition ratio was used, this being defined as $t_a - t_0/t_s - t_0$, where t_0 is the length of the induction period without the antioxidant, t_a and t_s are the lengths of the induction periods obtained with an arbitrary antioxidant at a given concentration, and that of a standard antioxidant at the same concentration, respectively. Lovern (3) and Simpson and Uri (4) used the ratio, $t_a - t_0/t_0$ in their work. However, these methods are not applicable to this investigation and the evaluation is based on the relative position of the oxygen uptake curve with respect to the control system curve. The lower the oxygen consumption for most of the period of 7 hr. the more efficient is the antioxidant at that concentration. The study was intended to show the relationship between the solubility of an antioxidant and its activity.

EXPERIMENTAL

Materials—The benzaldehyde, gallates, and cetomacrogol[1] were the same as those described in a previous paper (5).

Methods—*Measurement of Solubilities of Gallates in Water at 25°*—Saturated solutions of gallates were prepared by adding an excess amount of the gallate in distilled water in a glass-stoppered flask which was allowed to rotate in a thermostatically controlled water bath at 25 ± 0.05° for 24 hr. The amount of gallate in the filtrate was determined according to the B.P. method for the assay of propyl gallate (6). The filtrate from the dispersions containing octyl, decyl, and dodecyl gallates were concentrated due to the large volumes involved as these long chain members were sparingly soluble.

Measurement of Solubilities of Gallates in Cetomacrogol Solutions (0.04 M) at 25°—The same procedure as for the measurement of solubilities of aldehydes in cetomacrogol solutions was adopted (5), except that the end point was taken as the mean between a clear solution and one in which solid particles first appeared. This method could not be applied to ethyl gallate as turbidity appeared when the amount of ethyl gallate exceeded its water solubility. The turbidity increased with further additions of the antioxidant until a gel-like substance was formed, which separated out at the bottom of the container. This gel-like substance could be retained on a No. 5 sintered-glass filter. Assays of the filtrate showed that the amount of gallate present was equivalent to its solubility in water. When the filtrate was boiled no cloud point was observed. As a check, a saturated solution of propyl gallate in the same surfactant concentration was filtered through the same sintered-glass filter and its filtrate assayed. The propyl gallate content agreed with that determined by the visual method and cloud point was produced on boiling the solution. It is possible that ethyl gallate interacts with cetomacrogol to form an insoluble product and studies on this interaction are in progress.

Measurement of Solubilities of Gallates in Benzaldehyde at 25°—A series of predetermined amounts of the antioxidant were weighed into 2-ml. clear glass ampuls. One and one half milliliters of the aldehyde was added and the contents weighed. Oxygen-free nitrogen was bubbled into the ampuls which were sealed and placed in a thermostatically controlled water bath at 25 ± 0.05° for 24 hr. The end point was estimated in the same way as the above.

Measurement of Oxygen Uptake—This was determined using a Warburg apparatus and adopting the procedure of Mitchell and Wan (7). The systems investigated were the same as those stated earlier (5). In addition, emulsions were included, formed by adding excess aldehyde to the surfactant solution such that the ratio of the amount of aldehyde present to its solubility in the surfactant solution was 1:5.

RESULTS AND DISCUSSION

Methyl, ethyl, and propyl gallates are fairly soluble in water but octyl, decyl, and dodecyl gallates are practically insoluble. The gallate solubility increases with decrease in alkyl-chain length both in water and in cetomacrogol solutions except for ethyl gallate because of the interaction with the surfactant (Table I). The solubilities of octyl, decyl, and dodecyl gallates are very markedly increased in the surfactant solutions. This is likely to be related to the presence of a long hydrocarbon chain which may render them more readily solubilized in the hydrocarbon center of the micelle. In benzaldehyde, the solubility of the short chain gallates increase while that of the long chain members decrease with chain length of the alkyl substituent.

From Figs. 1–4, it can be seen that the induction period is distinct only with the long-chain gallates at low concentration in the solubilized system and therefore an assessment of antioxidant

Table I—Solubilities of Gallates in Water, Cetomacrogol Solution and Benzaldehyde at 25°C

Gallate	Water Solubility, moles/l.	Cetomacrogol Solubility,[a] moles/l.	Benzaldehyde Solubility, moles/mole
Methyl	6.0×10^{-2}	12.90×10^{-2}	2.0×10^{-2}
Ethyl[b]	5.9×10^{-2}	—	6.7×10^{-2}
Propyl	1.6×10^{-2}	11.10×10^{-2}	27.0×10^{-2}
Octyl	4.96×10^{-5}	4.96×10^{-2}	16.9×10^{-2}
Decyl	0.58×10^{-5}	4.77×10^{-2}	9.2×10^{-2}
Dodecyl	0.18×10^{-5}	4.08×10^{-2}	4.7×10^{-2}

[a] Cetomacrogol concentration = 0.04 *M*. [b] Ethyl gallate in cetomacrogol solution produces a gel-like substance when the gallate concentration exceeds the water solubility.

[1] Cetomacrogol 1000.

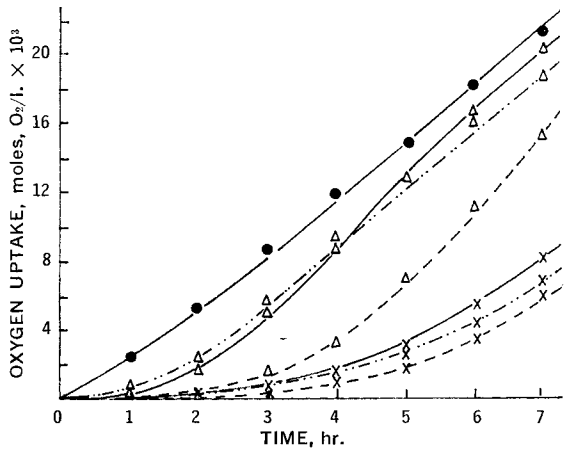

Figure 1—*Comparison of the efficiency of methyl, ethyl, and propyl gallates on the oxidation of benzaldehyde (0.1729 M) solubilized in cetomacrogol solutions (0.04 M) at 25° in the presence of cupric sulfate (1 × 10⁻⁴ M). Key: methyl,—; ethyl, - - -; propyl, - · - · - gallate Δ-1.2 × 10⁻⁴ M; ×-1.5 × 10⁻⁴ M; ●-control, without gallate.*

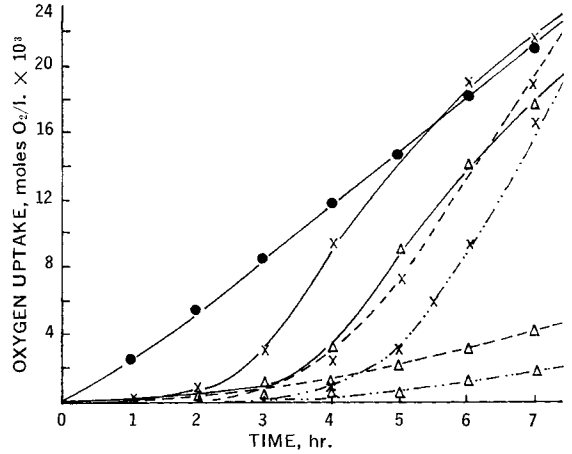

Figure 2—*Comparison of the efficiency of octyl, decyl, and dodecyl gallates on the oxidation of benzaldehyde (0.1729 M) solubilized in cetomacrogol solutions (0.04 M) at 25° in the presence of cupric sulfate (1 × 10⁻⁴ M). Key: octyl, —; decyl, - - -; dodecyl, - · - · - gallate ×-2.1×10⁻⁴ M; Δ-2.4 × 10⁻⁴ M; ●-control, without gallate.*

efficiency based on the measurement of the induction period would not be appropriate. However, by comparing the relative positions of the overall oxygen uptake curves of different gallates at the same concentration, the antioxidant efficiency can be estimated. In the solubilized systems (Figs. 1–2) the comparative antioxidant efficiency of the short-chain and long-chain gallates respectively is as follows: methyl < propyl < ethyl and octyl < decyl < dodecyl. This is generally true for the antioxidant concentration used ranging from 1.2 to 2.4 × 10^{-4} *M* for the short-chain gallates and 2.1 to 3.6 × 10^{-4} *M* for the long-chain gallates. The order appears to be related to the distribution ratios given in Table II. The distribution ratio for ethyl gallate cannot be calculated but it is expected to be higher than that of methyl or propyl gallate since it is likely that much of the gallate may be in the micellar phase as indicated by preliminary results from the current studies on this interaction. It appears that ethyl gallate interacts with the polyoxyethylene glycol portion of the surfactant. As more gallate is added to a cetomacrogol solution, an increasing amount of the gel-like substance is formed. The amount of ethyl gallate required to form the maximum quantity of gel increases with surfactant concentration and also with the chain length of the polyoxyethylene glycol. The interaction seems to be specific since similar types of surfactants selected so far have not exhibited this behavior.

The solubilized system has an aqueous phase and a micellar phase, both of which are saturated with respect to benzaldehyde, while the emulsified system contains in addition to these two phases, aldehyde globules which are stabilized by layers of adsorbed surfactant molecules. In these two systems, the added antioxidant probably distributes itself in each of the phases in accordance with its respective solubilities. The efficiency of a gallate on the aldehyde

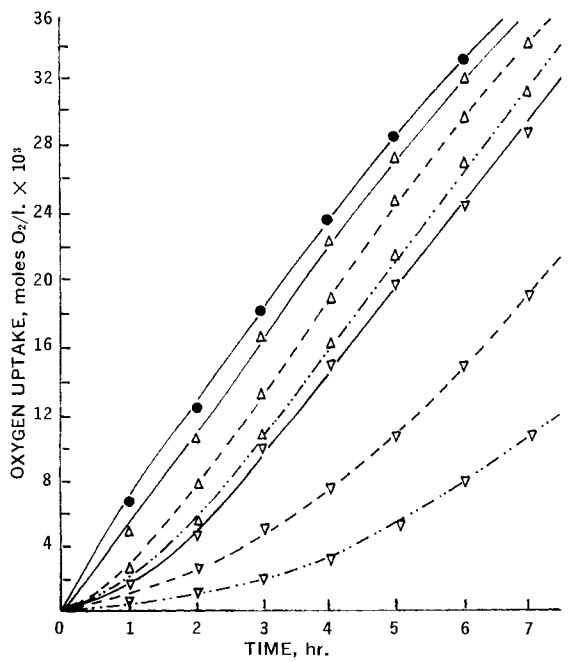

Figure 3—*Comparison of the efficiency of methyl, ethyl, and propyl gallates on the oxidation of benzaldehyde (0.2594 M) emulsified in cetomacrogol solutions (0.04 M) at 25° in the presence of cupric sulfate (1 × 10⁻⁴ M). Key: methyl, —; ethyl, - - -; propyl, - · - · - gallate Δ-1.8 × 10⁻⁴ M; ▽-3.6 × 10⁻⁴ M; ●-control, without gallate.*

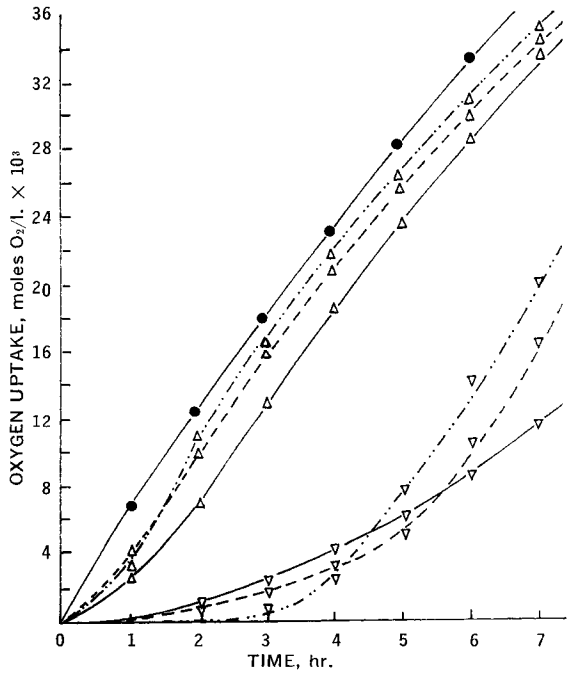

Figure 4—*Comparison of the efficiency of octyl, decyl, and dodecyl gallates on the oxidation of benzaldehyde (0.2594 M) emulsified in cetomacrogol solutions (0.04 M) at 25° in the presence of cupric sulfate (1 × 10⁻⁴ M). Key: octyl, —; decyl, - - -; dodecyl, - · - · - gallate Δ-1.8 × 10⁻⁴ M; ▽-3.6 × 10⁻⁴ M; ●-control, without gallate.*

Table II—Distribution Ratios of Gallates in Micellar Phase to the Whole Solubilized System Containing Benzaldehyde

Gallate	A. Solubility of Gallate in Aqueous Phase in 2 ml. of Reactant Solution	B. Total Solubility of Gallate in 2 ml. of Reactant Solution	C. = B−A Solubility of Gallate in Micellar Phase in 2 ml. of Reactant Solution	D. = C/B Distribution Ratio in Micellar Phase to Solubilized System
Methyl	1.2×10^{-4}	2.58×10^{-4}	1.38×10^{-4}	0.5349
Propyl	0.32×10^{-4}	2.22×10^{-4}	1.90×10^{-4}	0.8559
Octyl	9.92×10^{-8}	0.992×10^{-4}	0.9910×10^{-4}	0.9990
Decyl	1.16×10^{-8}	0.954×10^{-4}	0.9538×10^{-4}	0.9998
Dodecyl	0.36×10^{-8}	0.816×10^{-4}	0.8159×10^{-4}	0.9999

oxidation would be expected to depend on the solubility of the antioxidant in the phase where the main oxidation occurs relative to its total solubility in the system. In the calculation of the distribution ratios, it is assumed that the volume occupied by the micelles is small compared with that of the aqueous phase and their presence does not effectively reduce the volume of the aqueous phase which is taken to be equal to the total volume of the sample of the reactant solution. It has been shown that in solubilized systems (7) most of the aldehyde oxidation takes place in the micellar phase and practically no oxidation occurs in the aqueous phase. Hence for the antioxidant to exert its action it should be readily available in the micellar phase and the distribution ratio of the antioxidant is likely to effect the efficiency of the antioxidant. The gallates are much more soluble in the surfactant solutions than in water.

From a comparison of the relative positions of the respective oxidation rate curves (Figs. 3–4), the antioxidant efficiency in emulsified systems is as follows: methyl < ethyl < propyl and dodecyl < decyl < octyl. This order of efficiency is the same as that of the solubilities of gallates in benzaldehyde (Table I). For both the short-chain and the long-chain gallates, it is seen that the greater the solubility of the gallate in the aldehyde, the greater its efficiency as an antioxidant. In emulsions, oxidation occurs in both the aldehyde globules and in the micellar phase but the globules are believed to be the main site of action as they provide reservoirs of aldehyde for oxidation to take place. It is observed that in the absence of an antioxidant, the rate of oxidation in the control (Fig. 3) of the emulsified system is twice as great as that in the solubilized system (Fig. 1) although the quantity of aldehyde added is only one and one-half times that in the solubilized system. This means that when compared to the solubilized system a 50% increase in aldehyde present in the form of globules produces an approximately 100% increase in oxidation rate. In the emulsified system it is not known how much of the surfactant is available for micelle formation since an appreciable amount will be required for stabilizing the aldehyde globules. Hence the distribution ratios cannot be calculated.

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