Structure-Activity Relationships (SARs) of Antioxidant Molecules

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Abstract: The public's demand for antioxidant supplements has increased recently. As more of these supplements hit the market, an understanding of what makes a molecule a good antioxidant is paramount. The aim of this research project is to evaluate the antioxidant capacity of several phenols and related derivatives using the Briggs-Rauscher (BR) oscillatory reaction. The antioxidant species scavenge free radicals formed in the BR reaction, lengthening the time intervals of the reaction's oscillations; the higher the antioxidant capacity, the longer the oscillation delays. In phenol structures, the amount of hydroxyl (OH) groups affects the antioxidant capacity. By adding a hydroxyl group in a specific ring position, such as *ortho* or *para*, an increase of antioxidant capacity was observed. Previous research supports that *ortho* substitution of an electron donor increases the stability of the phenol radicals. Our results showed that *meta* substituted phenols were the most active antioxidants. We rationalize this observation by considering the low pH (~2) of the Briggs-Rauscher reaction. It was also noticed that a monophenol showed less antioxidant capacity than a polyphenol structure. Finally, we observed that the number of OH substituent does affect the antioxidant capacity.

Keywords: *antioxidants, oscillatory reaction, Briggs-Rauscher reaction, structure-activity relationship, and polyphenols.*

Introduction

Free radicals (FR) and reactive oxygen species (ROS) been suggested as potentially being important causative agents of aging and several human diseases such as cancer, inflammatory and degenerative diseases, emphysema, central nervous system injury, and autoimmune disease. The use of antioxidants for the prevention of damage caused by free radicals thereby assumes great importance for health and traditional medicine. Currently, there are many products on the market which claim to contain antioxidants.

The Briggs-Rauscher (BR) reaction is an oscillating reaction that changes between two cycles back and forth until it reaches equilibrium. The two cycles the reaction oscillates between correspond to a radical state and a non-radical state. The BR reaction is mostly used as demonstration.[1] Recently, Cervellati reported its use as a method to assess antioxidant capacity.[2] In this method, the presence of an antioxidant increases the oscillation time in the BR reaction. In this short communication we evaluate the antioxidant capacity of several phenols by using the Briggs-Rauscher reaction. We also determine structure-activity relationships within the tested phenol derivatives. A structure activity relationship shows how the feature of a chemical structure relates to the biological activity related with that specific chemical.

Methods and Results

A typical preparation of the Briggs Rauscher reaction was utilized.[3] When all stock solutions were prepared the solvents were tested as follows. Take 5mL of the sodium iodate solution, 5mL of starch solution, and 10mL 3% hydrogen peroxide. Once a stir bar has been placed in a 100mL beaker, start to mix the sodium iodate solution and starch solution in the beaker over a stirring plate. Then add the peroxide; the solution turns amber yellow then dark blue. Start the timer when the first dark blue color appears until the next dark blue appears. This is the oscillation time (usually 13-18 seconds). This is also the control time for each trial. Repeat the step above and when the second deep blue color appears, add 1mL of antioxidant solution. Measuring the time from the second blue to the third blue appearance determines the antioxidant performance.

Throughout our experiment there were some phenols that were tested that did not have any antioxidant activity. Cinnamic acid, p-coumaric acid, and p-hydroxybenzoic acid, had minimal affect; however, the oscillation delay was not consistent throughout the trial. SARs were present in each phenol structure.[4] The phenol with the hydroxyl substituent in the meta position showed the greatest antioxidant activity (Figure 1). Among the phenol derivatives, pyrogallol, and resorcinol were the most active antioxidants. Since resorcinol has the hydroxyl group in the meta position, it exhibited the most antioxidant activity. In the phenol acids, the most active antioxidants were caffeic acid and gallic acid. Gallic acid contains 3 OH groups with a carboxylic acid attached directly to the ring. However, caffeic acid showed to be more active than gallic acid even though it has two OH groups attached to the ring. The studied polyphenol molecules contained aromatic and phenolic rings that possess some patterns mentioned earlier, such as multiple OH substituents in specific positions. The most active that was tested in this experiment was quercetin, which exhibited these specific patterns. Finally, some of the samples lost antioxidant activity with exposure to air and light.

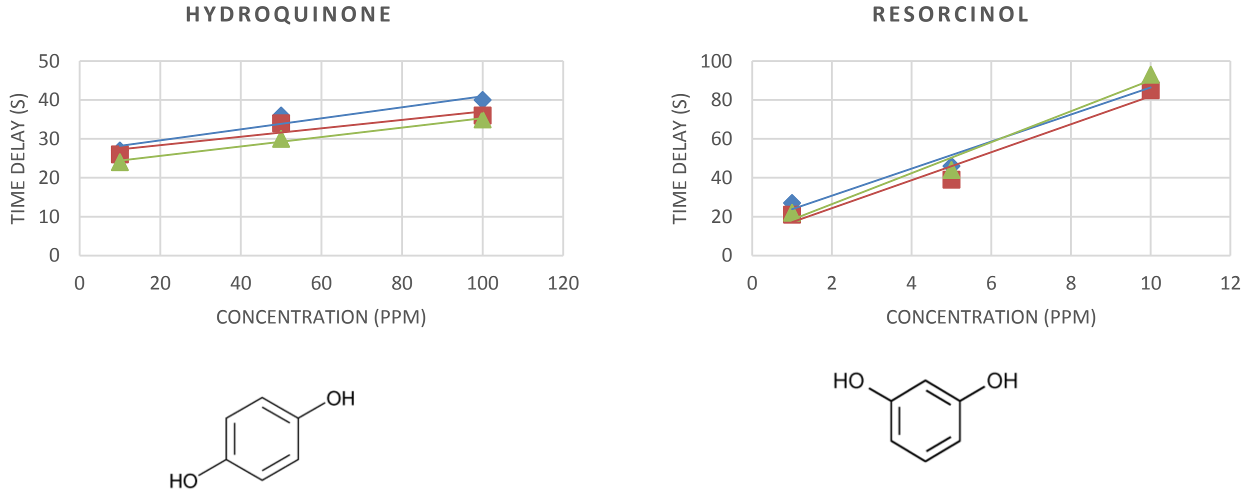

Fig. 1: (Left) Antioxidant performance of hydroquinone. (Right) Antioxidant performance of resorcinol. The steeper slope indicates more antioxidant activity.

Conclusions

The Briggs-Rauscher oscillating reaction is effective assessing antioxidant performance. We consistently observed that OH substituents affect antioxidant activity. Hydroxyls located in the meta position exhibited the greatest antioxidant activity. In the future, we aim to develop a more encompassing SAR for antioxidant molecules.

Conflicts of Interest

The authors declare no conflict of interest.

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References and Notes

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