# A PRESCRIPTION CONTAINING GUAIAC AND ACACIA.*

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## INTRODUCTION.

Mixtures containing the resinous tincture of guaiac have occupied a prominent place in the teaching of prescription incompatibilities for many years. The proper compounding of prescriptions containing various quantities of tincture of guaiac, honey, acacia, potassium chlorate and water require an exercising of the pharmaceutical art of compounding. From a retail pharmacy in Baltimore the following prescription was brought to the attention of one of the authors:

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| Tinct. Guaiaci | 15 |
| Mel Depurati | 15 |
| Kali Chlorati | 13 |
| Syr. Acaciae q. s. | 90 |
| *Misce et pone in solutio* | |

This prescription had been compounded several times according to the generally excepted procedure, producing upon each occasion the characteristic pinkish red coloration of a guaiac mixture. The next time the prescription was filled, presumably in the same manner as before, the mixture developed during the course of compounding a bluish green color. Four additional attempts at compouding, modifying the methods of mixing with the same ingredients, produced the bluish green color.

The authors decided to subject the mixture to a scientific investigation in order to determine the nature of the color change.

## HISTORICAL.

The pharmaceutical literature is replete with records of work which has been carried out in studies of the constituents of guaiac and some of its color reactions. E. Schaer (1) determined that guaiac resin contained 70 per cent of guaiaconic acid and 10 per cent of guaiacresinic acid. The former produces the characteristic blue with oxidizing agents, whereas the latter does not react in this way. This same investigator observed that the exposure of guaiaconic acid to sunlight brought about a molecular rearrangement of the compound rendering it inactive in the presence of oxidizing agents. Atkins (2) observed that certain metallic ions interferred with the guaiac test for oxidases by reacting with the guaiaconic acid to produce the blue color thus vitiating the test. Sartory (3) confirmed the observations of Atkins pointing out that potassium permanganate and cupric salts reacted with guaiaconic acid to produce the characteristic blue color. Schaer (4) observed that alkalies and alkali-carbonates decolorize guaiac-blue and prevent its formation, which he believes to be an ozonide of guaiaconic acid.

A recent study of acacia by Tschirch and Flück (5) has shown this gum to contain certain oxidases. The Pharmacopei Helvétique makes provisions for the destruction of the oxidase in the gum by the boiling of a solution of the product for ten minutes. Various methods of inactivating the oxidase were described

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recently by M. Mascré (6), these consist essentially of boiling the aqueous solution of the gum or treating the dry gum for one hour with boiling salcohol.

## EXPERIMENTAL.

This prescription was compounded with a powdered gum arabic of U. S. P. quality. The characteristic blue color developed. The hydrogen-ion concentration of the mixture was measured electrometrically by means of the quinhydrone electrode. The $p_H$ of the mixture was 4.42. The mixture was prepared omitting the potassium chlorate and the blue color appeared as before. Including the potassium chlorate and omitting the acacia, no blue color developed, likewise it was shown that honey was not responsible for the color change. This seemed to indicate that acacia was responsible for the oxidation of the guaiaconic acid.

The prescription was compounded with all of the ingredients in addition to 1 per cent hydrochloric acid—the $p_H$ of this was 0.48 and no blue color developed indicating that in a high hydrogen-ion concentration the oxidase is inactivated. In order to ascertain the influence of a solution containing a lesser hydrogen-ion concentration, the mixture was prepared in 0.01 *N.* hydrochloric acid and 1 per cent acetic acid, respectively. The $p_H$ of the former was 3.32 and that of the latter was 3.71. In neither of these products did the blue-green coloration appear indicating the inactivation of the oxidase with these degrees of hydrogen-ion concentration.

The mixture was prepared containing 1 per cent potassium bicarbonate, 1 per cent potassium carbonate and ammoniated tincture of guaiac, respectively.

| | | |
|---|---|---|
| With $KHCO_3$ | — | $p_H$ about 8.4 |
| With $K_2CO_3$ | — | $p_H$ about 11.6 |
| With $NH_4OH$ | — | $p_H$ about 11.3 |

Not any of these products developed the blue color, however, the usual pink coloration was replaced by a brown color. This confirms Shaer's observation that alkalies prevent the formation of the guaiaconic acid oxidation product.

The solution of acacia was boiled for fifteen minutes before introducing it into the prescription. No blue-green color developed which indicated the inactivated oxidase as described by Mascré. This was repeated several times and in none of these mixtures did the oxidation of guaiaconic acid occur.

In order to ascertain the influence of boiling upon the hydrogen-ion concentration of the acacia solution, 6 Gm. was dissolved in enough water to prepare 90 cc. The $p_H$ of this solution, measured by means of the hydrogen electrode, was 4.45. This value is in close agreement with the work of Schwartze *et al.* (7) and that of the first author (8). The solution was boiled for twenty minutes, allowed to cool, and the hydrogen-ion concentration was measured. This value was $p_H$ 4.42. This experiment indicates that boiling does not influence the $p_H$ of the acacia solution and it is not this reason that boiling prevents the formation of the blue-green color.

Considering the conclusion of Shaer, that guaiaconic acid underwent molecular rearrangement upon exposure to light and became inactive in the presence of oxidizing agents, the following experiment was performed. A sample of tincture of guaiac was exposed to ultraviolet light (Alpine Sun Lamp 12 inches from the

mercury arc in quartz) for a period of thirty minutes. This sample as well as a control were used to prepare the guaiac-mixture prescription. In each the blue-green color developed simultaneously and approximately to the same degree. From the work of Shaer one might have expected this treatment with ultraviolet light to prevent the formation of the oxidation product of guaiaconic acid. Under the conditions mentioned, the authors found no influence upon the color formation after irradiation with ultraviolet light.

## CONCLUSIONS.

1. The blue-green color formed in the mixture described in this paper is due to the action of the oxidase in acacia upon one of the constituents in tincture of guaiac.

2. The oxidation and accompanying color change can be prevented by inactivating the oxidase in acacia by boiling a solution of the gum for twenty minutes.

3. Modifying the mixture so as to change the hydrogen-ion concentration to a $p_H$ below 3.71 or above 8.4 prevents the formation of the blue-green color.

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## ABSTRACT OF DISCUSSION.

In reply to the question by **John Culley**, what the objection was to the green color—**Dr. Krantz** stated that he did not investigate the therapeutic activity, but the patient did not accept the refilled prescription, because the color of the preparation was not like that of the first preparation.

**E. Fullerton Cook** thought the difference in color was due to the age of the preparation.

**C. M. Snow** inquired how far a pharmacist could go in making changes that would not affect the therapeutic activity. He asked to be informed on the subject under discussion—as acacia is the disturbing factor, the component being syrup of acacia; also, as powdered acacia, usually, does not contain the ferment—whether substitution of simple syrup for syrup of acacia would be permissible.

**William Gray** inquired whether Dr. Krantz considered that the guaiac had a part in the variation of color reaction.

**Dr. Krantz** replied that three different guaiacs were used in an effort to obtain the coloration of the first preparation—one from the original sample; one an old guaiac, purchased from a retail pharmacist; and another from a fresh sample. Invariably a greenish color was obtained, with slight difference in shade. The greenish color developed when the acacia solution was not heated, but not when the solution was boiled—the color varied in degree of intensity.

**William J. Husa** expressed the opinion that the oxidase had no therapeutic value in the preparation and, hence, no harm is done by destroying the ferment as far as medicinal value is concerned; but if the acacia is left out of the prescription there would be a change in the preparation which might not be permissible.

**A. O. Mickelsen** questioned the right to destroy the oxidase and thus change the prescription.

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