

## SCIENTIFIC SECTION

### DETERIORATION OF CERTAIN MEDICAMENTS UNDER THE INFLUENCE OF LIGHT.

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#### PECULIARITIES OF THE INDIVIDUAL CHEMICALS.

*Adrenalin Hydrochloride*.—While amber bottles are the only type that preserve the solution when cork stoppers are used, ampuled solutions keep under all light conditions for a period of one year.

*Apomorphine Hydrochloride* solutions deteriorate even in the dark. Ampuled solutions darken if air is above the liquid. When CO<sub>2</sub>-filled, the ampuled solutions keep under all light conditions.

*Benzoic Acid* keeps perfectly in amber-glass containers during exposure to direct daylight during a period of one year. In bottles of other colors and in colorless containers discoloration begins within six months. In diffused light, samples keep without discoloration for over one year, regardless of the color of the container.

*Betanaphthol*.—In direct daylight, all samples in all types of containers were discolored within two months of exposure. In diffused light, and stored in amber A and B and in Green B containers the chemical was not discolored after one year of exposure.

*Chloroform*.—Amber A and B and Green B containers afforded protection in direct daylight for a period of twelve months. Other types of bottles were less effective. In diffused light, all containers preserved the chemical over a period of twelve months.

*Ephedrine Hydrochloride* solutions in cork-stoppered containers will not keep except when stored in the dark. Darkening, however, is evidently due to oxidation. Ampuled solutions keep under all light conditions.

*Ether*.—No type of transparent container kept the two U. S. P. samples of this chemical studied by us longer than two months when exposed to direct daylight. In most cases after two months of storing in cork-stoppered bottles the samples had evaporated. Again, we note that even under these severe conditions Amber A and B and Green B containers afforded the most effective protection. In diffused light, samples stored in Amber A and B and Green B containers kept perfectly for one year.

*Ferric Citrate*.

*Ferric Phosphate, Soluble*.

*Ferric Pyrophosphate, Soluble*.

All three of these scale salts of iron changed color after exposure to direct daylight for one month, regardless of the type of glass container used. In diffused light, Amber A and B and Green B preserved ferric pyrophosphate for over one year; Amber A and B preserved ferric phosphate for one year; whereas ferric citrate after exposure for six months in any container became darker in color.

Stored in the dark in any container the color of these salts remained unchanged during the year of observation.

*Hydriodic Acid, Diluted.*

*Hydriodic Acid, Syrup.*

*Hydrobromic Acid, Diluted.*

These three products, all of the quality prescribed by U. S. P. X or U. S. P. IX, maintained their full halogen content even after one year of exposure to direct daylight or to diffused light. In the case of diluted hydrobromic acid, no darkening resulted from exposure to light. The iodide preparations did darken in direct daylight; all samples darkening between the fourth and sixth months of exposure except in the case of flint glass and the amber containers where the sample of the acid remained colorless for about twelve months. The syrup exhibited the same peculiarities as syrup of ferrous iodide, which will be discussed below.

*Hydrocyanic Acid, Diluted.*—This product exhibited peculiarities which were quite puzzling until our experiments finally convinced us that loss in cyanide content was not due to light, but to volatilization.

*Mercuric Iodide* kept perfectly for one year all under conditions of light exposure and when stored in all types of glass containers used by us.

*Mercuric Oxide, Red.*—None of the type containers studied afforded this chemical protection against direct daylight or diffused light. Within one month, all of the samples had darkened. Storage in the dark is the only practical means of preservation.

*Mercuric Oxide, Yellow.*—In direct daylight, all samples in all types of glass containers used, darkened within one month of exposure. In diffused light, Amber B and Green B containers preserved the chemical for over one year.

*Mercurous Chloride.*—In direct daylight, calomel remained unchanged in color for one year when stored in Ambers A and B and Green B containers. Stored in the other containers darkening took place within one month. In diffused light, no darkening occurred to the chemical, when stored in any of the containers used; even after exposure for one year.

*Mercurous Iodide.*—The light-sensitivity of this salt is known to all chemists and our study of this erratic chemical is worthy of a special paper. At this time we will summarize our findings as follows: (a) Under all conditions of light in all types of containers studied, the salt darkens within one month; (b) It keeps perfectly for twelve months or more when stored in the dark; (c) The blackening is a surface phenomenon only and the black film protects the inner layer of chemical from the light; (d) A sample kept in diffused light and shaken from time to time eventually developed some indications of the red tint of mercuric iodide; (e) Assay of said sample, however, indicated but little change in the HgI content of the gray and the reddish portions; (f) No indications could be noted of the presence of free iodine in the darkened samples.

*Phenol, Liquefied.*—The first sample obtained and observed for one year exhibited erratic behavior. A second sample observed for six months was stable under all conditions. The latter product is popularly supposed to contain a stabilizing catalyst.

*Physostigmine Salicylate* solutions act in an erratic fashion. They are fairly stable when stored in ampuls with CO<sub>2</sub> atmosphere.

*Pyrogallol.*

*Resorcinol.*

These chemicals, exposed to direct daylight, keep well for about one year when stored in Amber A and B and Green B containers. In diffused light, they keep for one year or more in any of the containers used by us.

*Santonin*, when exposed to direct daylight turns yellow in less than two months when stored in any of the glass containers we used. In diffused light, Amber A and B and Green B containers preserved the chemical in a colorless condition for one year or more.

*Silver Nitrate.*—In all cases where darkening occurs, gray specks begin at the top. It is claimed that chloride-free silver nitrate does not turn gray and our observations confirm this statement. The darkening (when occurring) is apparently partly due to traces of chlorides absorbed from the air. Light seems to play an unimportant rôle, since the control samples kept in the dark turned gray as quickly as those samples exposed to diffused light. As to the preservative action of colored glass, samples stored in Amber A and Green A and B containers kept perfectly for 12 months in diffused light.

*Silver Proteins.*—Samples of both the "strong" and "mild" varieties were studied with careful checkings of the pAg value of the solutions when fresh, when kept in the dark and when exposed to direct daylight in the various types of glass containers used by us. Our figures indicate that little or no change in silver-ion concentration occurs, since the pAg remains fairly constant over a period of one year. However, from the standpoint of physical appearance, solutions should be stored in amber containers, as slight depositions of metallic silver were noted on the walls of the other types of bottles after four months' exposure to direct daylight.

*Solution of Arsenous and Mercuric Iodide.*—Careful work on this solution has recently been reported by Rosin and by Husa. Our conclusions may therefore be condensed to the bare statements: (a) That even when stored in the dark, the solution is unstable; (b) That in diffused light, amber containers afford the best protection; (c) That yellow color, due to free iodine, does not appear until practically all of the arsenous iodide is converted into the arsenic form.

*Solution of Chlorinated Soda.*—Even when stored in the dark, this solution loses about one-third of its active chlorine content within twelve months. The same solution stored in Amber A and B and in Green B containers in direct daylight lost ten per cent within one month; while all samples stored in other glass containers lost from fifty to eighty per cent during the same period. In diffused light, all of the samples (except those in flint glass) kept about as well as the samples kept in the dark. This would seem to indicate that deterioration in the case of this solution is due to volatilization.

*Solution of Chlorine, Compound.*—This notoriously unstable product decomposes with great rapidity when exposed to direct daylight and even when stored in the dark it loses about one-third of its chlorine content within two weeks. On the other hand, *chlorine water* prepared by saturating distilled water with the gas, keeps its full strength for six months when stored in the dark. This type of

solution is decomposed by direct daylight regardless of the type of container in which it is stored.

*Solution of Hydrogen Dioxide.*—Two samples were studied during a year. "A" states upon the label that it contains  $\frac{1}{8}$  grain of acetanilid per ounce. "B" is free from acetanilid but we understand that it does contain traces of a stabilizing catalyst. "A" stored in Amber B container exposed to direct daylight kept its strength for two months. Stored in other types of bottles it deteriorated within one month. "B" stored in Amber A and B and Green B containers in direct daylight retained its strength for two months. In diffused light, Amber A proved the best container. Both solutions deteriorated slowly when stored in the dark; the  $H_2O_2$  loss in both samples when stored in the dark one year being less than 10 per cent.

*Spirit of Ethyl Nitrite.*—Much work was performed on this pharmaceutical. Amber bottles kept it for from one to two months when exposed to direct daylight, whereas in the dark the loss in nitrite was about sixteen per cent in twelve months. In diffused light, figures obtained were so erratic that we are inclined to the belief that deterioration is due to evaporation of the nitrite rather than to the influence of light. We were also unable to find much difference in deterioration between samples made by dissolving the nitrite in Alcohol U. S. P. or in absolute alcohol.

*Sulphurated Potassa.*—Although the color of the sample had changed from liver-brown (when freshly prepared) to greenish yellow, after exposure to air for a few hours and although it remained this green-yellow color after one year of exposure to direct daylight, all samples at the end of the year kept within the U. S. P. assay requirements. Light seemed to play no part in this color change; for deterioration (as to color) went on in the dark as well as in sunlight regardless of color of glass container. We therefore believe that the deterioration is an oxidation rather than a light phenomenon.

*Syrup of Ferrous Iodide* is the subject of a special paper read by us at the 1931 meeting of the New York State Pharmaceutical Association. As in the case of the hydriodic preparations mentioned above, the iodide content remained constant through twelve months, regardless of light conditions or type of glass container. The darkening of this syrup is due to the action of the hypophosphorous acid mistakenly added as a preservative. This chemical does preserve the syrup for two or three months, after which it assumes a permanent brown color. Samples made without hypophosphorous acid turn brown within a few days, but exposure to sunlight for a few hours restores its original green color.

*Thymol Iodide.*—None of the types of glass containers used protected this chemical from deterioration from direct daylight although those samples stored in Amber A and B and Green B containers remained unchanged for four months. Stored in the dark, the color of the product remained unchanged during a period of over one year. In diffused light, samples stored in all of the glass containers except flint glass kept as well as those kept in the dark.

#### EXPERIMENTS WITH STABILIZERS.

In the case of the following chemicals the influence of certain stabilizers was studied.

TABLE IX.

Chemical (or preparation).	Stabilizers tried.
Betanaphthol	Citric acid, terpin hydrate, stannous chloride, colloidal copper, colloidal tin oleate
Ether	Colloidal copper, colloidal tin oleate tin foil plus copper gauze
Ferric citrate	Sodium citrate, sodium biphosphate, stannous chloride, terpin hydrate, colloidal copper, colloidal tin oleate
Ferric phosphate, soluble	
Ferric pyrophosphate, soluble	
Hydriodic acid, diluted	
Mercuric oxide, red	See betanaphthol
Mercuric oxide, yellow	See betanaphthol
Mercurous iodide	See betanaphthol
Phenol	Sodium sulphite. Also see betanaphthol
Pyrogallol	See betanaphthol
Resorcinol	See betanaphthol
Solution of arsenous and mercuric iodide	See betanaphthol
Solution of hydrogen dioxide	See betanaphthol
Solution of chlorinated soda	Saccharin, sodium chloride
Spirit of ethyl nitrite	Sodium carbonate, calcium chloride "Mollit" and "Anhydrone"

These stabilizers were picked more or less at random from chemical preservatives suggested in the literature. None gave satisfactory results in our hands except the well-established facts that tin compounds stabilize phenol and that acetanilid is a fairly satisfactory preservative for solution of hydrogen dioxide. It is an interesting fact, however, that stannous chloride exerts a distinct stabilizing influence on peroxide solutions.

## OTHER COLORED GLASSES.

Our investigation was planned for a study of *glass containers which are actually available in the American market*, hence the study of special types of colored glass in sheet form scarcely belonged in our field of work. However, during the past few years there has been placed upon the market standard types of colored glass and as spectro-photometric readings indicated that glass of red tint should be the best protection for light-sensitive chemicals, we devoted a small portion of our time to this problem. The six "Corning color filters" selected were (a) "Pyrex" (b) "Nultra" (c) Lantern Blue (d) "Noviol" (e) Sextant Green and (f) Heat-resisting Red. These were fitted as "windows" to small "cameras" so that light could penetrate only through the glass plate. The chemicals in the pyrex test-tubes, already described, were placed within these "cameras" and were then exposed to direct daylight for a period of four months when the "cameras" were opened and the chemicals were either assayed or examined as to color changes.

Table X gives the results of this study.

TABLE X.—CORNING FILTERS.

(4 Months' Exposure.)

Chemical.	Glass preventing deterioration.
Betanaphthol	Red and green
Ferric citrate	Red and green
Ferric phosphate, soluble	Red and green
Ferric pyrophosphate, soluble	Red and green

TABLE X.—*Continued.*

(4 Months' Exposure.)

Chemical.	Glass preventing deterioration.
Hydriodic acid, diluted	All
Mercuric oxide, red	Red
Mercuric oxide, yellow	None
Mercurous iodide	None
Phenol	Red and green
Pyrogallol	Red, green and "Noviol"
Resorcinol	Red, green and "Noviol"
Santonin	Red and green
Solution of chlorinated soda	Red and green
Solution of hydrogen dioxide	Red, green and "Noviol"
Spirit of ethyl nitrite	Red, green and "Noviol"

## BIBLIOGRAPHY.

Dr. Steinberg's dissertation gives a bibliography of 197 titles. Limitations of space prevent our publishing it in this article.

## CONCLUSIONS.

(1) Spectral transmission curves of the eight samples of glass containers used as well as six samples of Corning glass filters are given.

(2) Reports are made on the deterioration of 35 chemicals and preparations stored in seven of the types of containers mentioned above under the following conditions: (a) exposed to direct daylight, (b) exposed to diffused light, (c) kept in a dark closet in "dark room." Since Amber C container closely resembled Amber B container, it was not used in all of our work.

(3) These exposure tests indicated that Amber A and B and Green B containers were the best protectives for light-sensitive chemicals. The other bottles used afforded poor protection against light rays.

(4) Of the 35 chemicals and preparations studied, all did not deteriorate because of the action of light. Other factors were: (a) Atmospheric oxidation: examples, apomorphine hydrochloride, sulphurated potassa and phenol. (b) Evaporation: examples, spirit of ethyl nitrite and diluted hydrocyanic acid. (c) Other atmospheric impurities: example, silver nitrate.

(5) Direct sunshine was very destructive to light-sensitive chemicals. In diffused light (resembling drug store conditions) the deterioration was much less (one-third to one-twelfth); in fact, with most chemicals, not much more than when the chemical was kept in a dark place.

(6) Reports on the protective action of certain stabilizing catalysts and of special types of colored glass are given.

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## EXPLORING ECONOMIC PLANTS.\*

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Few fields create as much interest and offer as much fascination and satisfaction as does the exploration of the marvels and mysteries of economic plant life.

The dynasty of drug plants dates back to the days of the forefathers of prehistoric life. There is little doubt that the evolution of many plants into present-day forms has been greatly facilitated by the advent and progress of all worldly

\* This paper is an elaboration of part of a comprehensive survey of the native plant resources of the Pacific coast. Scientific Section, A. PH. A., Miami meeting, 1931.

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