While this method is not theoretically correct, there probably being some dissolved camphor and chloroform in the aqueous-alcoholic layer and *vice versa*, the practical application seems to be correct.

CONCLUSIONS.

Only slight decrease was noted in the chloroform content of chloroform liniment over a ten-day period and even on the three-month period, under conditions of extreme temperature, a maximum loss of only 3.8% was noted; also, quite contrary to expectations, there was no appreciable difference between the stability in glass- and cork-stoppered containers.

It seems, therefore, that the charge of unfairness in selecting such a sample as a test sample is not borne out. First, such a preparation would not normally be kept on the shelves of the average pharmacy for a period of three months. Second, if there is but little call for it the desired quantity can easily be prepared in a few moments.

It seems, therefore, that observed variations of five, and, in some cases ten per cent., cannot be justifiably excused.

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SOME PHYSICAL AND CHEMICAL PROPERTIES OF NEOROBIN.*

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I. INTRODUCTION.

Schamberg and Raiziss,[1] of the Dermatological Institute, Philadelphia, have introduced a new remedy in the treatment of psoriasis, pityriasis capitis, and some other forms of skin eruption, to which they have given the name Neorobin. Neorobin is a derivative of Chrysarobin and is made by dissolving the latter in glacial acetic acid and subsequent reduction with metallic tin.

Chrysarobin has been used quite extensively in the local treatment of psoriasis. On account of its marked staining properties, Schamberg and Raiziss have developed Neorobin which does not stain as markedly as Chrysarobin, and is more active as a reducing agent. Since Neorobin is gradually oxidized on exposure to the air, it is marketed in the form of a powder in tubes, flame-sealed under vacuum. When ready for use the powder is made up into an ointment which is then applied to the skin.

The purpose of this investigation was to devise physical and chemical tests for Neorobin which would differentiate it from Chrysarobin. It is needless to state that synthetic remedies or pharmaceuticals should be standardized or scientifically controlled whenever possible. This insures "therapeutic efficiency" and serves as a confirmatory identity test for the product. It is true that tentative assay methods of plant products and principles are often only approximate but are undoubtedly superior to empirical facts.

Most dermatologists attribute the therapeutic value of Chrysarobin in skin diseases to its reducing properties. As Neorobin has proved to be more active clinically than Chrysarobin, we have attempted to determine the relative reducing

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power of the two and thus correlate this reducing action with therapeutic efficiency. A quantitative measure of the reducing power serves, therefore, not only to differentiate Chrysarobin from Neorobin but also as a means of standardizing different lots of Neorobin.

II. PHYSICAL PROPERTIES.

Neorobin is a yellow or yellowish gray powder. According to Schamberg and Raiziss it melts at approximately 190° C. They also state that it is slightly soluble in ether and methyl alcohol, and more soluble in glacial acetic acid, chloroform, benzene, and ethyl alcohol. In addition to these solvents, acetone was found to dissolve Neorobin and Chrysarobin quite readily. The former produces a golden yellow and the latter a dark red solution. No quantitative solubility tests were made with this solvent, but it was found that Chrysarobin yields 0.002 Gm. and Neorobin 0.004 Gm. of insoluble matter per gram sample. About one-quarter of the insoluble matter in Neorobin is silica.

The ash standard for Chrysarobin is 0.25%. The average percentage of ash in Neorobin has been found to be 0.6%.

Both Neorobin and Chrysarobin give a residue on subliming but the microscopical examination shows no distinguishing structure. Crystallization of Neorobin from glacial acetic acid, benzol, alcohol, xylol, benzene, and methyl alcohol was tried but with little success. A 0.1% solution of Neorobin or Chrysarobin in acetone gives crystals which have a tendency to change to the compound form. Neorobin crystallizes under certain conditions in chain formation. Sheath-like crystals are also seen. Chrysarobin forms crystals much more slowly which are relatively larger and darker in color. Compound crystals are not nearly so prevalent.

III. CHEMICAL PROPERTIES.

Neorobin is very slightly soluble in water. An aqueous suspension is neutral to litmus. Fixed alkalies dissolve Neorobin forming a deep red-colored solution. When boiled with sodium carbonate a deep red solution is also formed. Fuming nitric acid produces a red mixture which turns violet-red on the addition of ammonium hydroxide.

The method of preparation of Neorobin suggested the possibility that the substance was a complex acetate. Three gram samples of Neorobin were suspended in water to which was added phosphoric acid and silver sulphate, and the whole distilled. The distillate was negative for acetates with the sulphuric acid and ferric chloride test. Titration with alkali showed a negligible trace of some volatile acid. An analysis of the ash of Neorobin showed no tin present. These tests show that Neorobin is primarily a reduction product of Chrysarobin and is neither a compound of tin nor an acetate.

The known reducing action of Chrysarobin and Neorobin suggested a possible quantitative measure of this property. After considerable thought, acetone was chosen as the best solvent for this purpose. The color of the acetone solution and the formation of colored compounds eliminated some possible methods. The method finally adopted consisted in adding ammoniacal silver nitrate in excess to an acetone solution of the substance, whereby the silver nitrate was reduced to metallic silver and the latter determined quantitatively. This method was used to advantage by Smith[2] in the estimation of sodium hyposulphite.

IV. PROCEDURE FOR DETERMINING THE REDUCING POWER OF NEOROBIN AND CHRYSAROBIN.

(*a*) *Reagents.*—(1) Freshly prepared ammoniacal silver nitrate solution.

$AgNO_3$ C. P.	3 Gm.
NH_4OH (10%)	10 cc
Dist. H_2O	120 cc

(2) Ammoniacal solution of ammonium nitrate.

NH_4NO_3 C. P.	15 Gm.
NH_4OH (10%)	10 cc
Dist. H_2O	300 cc

(3) Acetone C. P. The acetone must pass all the tests given in the U. S. P. and in Merck's "Chemical Reagents and Their Purity Tests," 2nd Edition.

(*b*) *Procedure.*—Weigh accurately 0.1 Gm. of Neorobin or Chrysarobin. Place in a large beaker and add 50 cc of acetone. As soon as the substance dissolves add 10 cc of the ammoniacal silver nitrate solution. Allow to stand two hours until the Neorobin or Chrysarobin is completely oxidized. The precipitated metallic silver is then filtered on a Gooch crucible. An excess of asbestos interferes with the washing and filtration of the precipitate and must be avoided. The precipitate and beaker are washed repeatedly with ammoniacal ammonium nitrate solution until free from silver salts. The ammoniacal ammonium nitrate solution is used to retain the finely divided silver on the Gooch. About 150 cc is used to wash the precipitate free from silver nitrate. The Gooch is placed in the same beaker in which the reaction took place and the silver dissolved with 10 cc of nitric acid. An excess of nitric acid should be avoided as it interferes with the Volhard titration. Enough distilled water is added to cover the crucible and the whole boiled for about twenty minutes to insure complete solution of the silver and to remove any nitrous acid formed. After cooling remove the Gooch and filter the solution through filter paper. Wash with distilled water until the filtrate gives a negative test for nitrates with diphenylamine. The final volume is about 350–400 cc. The solution is yellow but it does not interfere with the Volhard titration. Ferric alum T. S. (1 cc) is used as the indicator and the solution is titrated with 0.1 *N* KCNS. As the KCNS is added the precipitated AgCNS turns the solution a milky white and as the end-point is reached the AgCNS coagulates. The end of the reaction is taken when the solution assumes a reddish brown color by transmitted light and pink by reflected light. When C. P. chemicals are used in this assay, a blank determination has been found to be unnecessary.

EXPERIMENTAL DATA.

TABLE 1.

Grains of Silver Reduced by 0.1 Gm. Sample of Neorobin or Chrysarobin.

Neorobin.		Ag.	Chrysarobin.		Ag.
Lot	1	0.1337	Lot	1	0.0819
	2	0.1370		2	0.0798
	3	0.1262		3	0.0809
	4	0.1337		4	0.0830
	5	0.1348		5	0.0863
Average		0.1330	Average		0.0823

The samples of Neorobin used in this test were actually taken at random from five distinct commercial lots. The samples of Chrysarobin came for various sources. They are, therefore, fairly representative samples.

The results of Table 1 show quite clearly that Neorobin reduces at least 50% more ammoniacal silver nitrate than Chrysarobin. This increased reducing power of Neorobin may be theoretically accounted for if we consider the chemistry of Chrysarobin. As ordinarily prepared Chrysarobin contains varying amounts of chrysophanic acid. In an alkaline solution, Chrysarobin is easily oxidized to chrysophanic acid due to the absorption of oxygen from the air. Liebermann has shown that Chrysarobin has the chemical structure of a reduced quinone, whereas chrysophanic acid is a dioxy-methylanthraquinone. Therefore, the power of Chrysarobin to absorb oxygen is due to the presence of the reduced quinone group which is oxidized to chrysophanic acid.

Neorobin is a reduction product of Chrysarobin. It is quite probable that the chrysophanic acid naturally present in Chrysarobin is reduced, thus increasing the reducing power of the substance as a whole. In other words, the greater reducing action of Neorobin is due to the presence of a quinone which has been partly produced by the reduction of chrysophanic acid in Chrysarobin. In our opinion this explains the greater affinity of Neorobin for oxygen.

V. CONCLUSIONS AND SUMMARY.

Neorobin dissolves readily in acetone producing a golden yellow solution. Chrysarobin also dissolves easily in the same solvent but forms a dark red solution. This difference in color in acetone is important as this fact can be utilized as a simple differentiating and identity test for Neorobin and Chrysarobin.

Neorobin is primarily a reduction product of Chrysarobin and is neither a tin compound nor a complex acetate.

Using the reduction of ammoniacal silver nitrate as a criteria of reducing power, Neorobin is at least 50% more active as a reducing agent than Chrysarobin.

If, as is generally admitted, the therapeutic action of Chrysarobin is primarily due to its reducing action, then Neorobin should be at least 50% more active therapeutically.

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LEECHES—HOW TO DISPENSE THEM.*

BY OTTO RAUBENHEIMER.

The leech, Latin *Hirudo*, plural *Hirudines*, has been used since the earliest times. Family quarrels then, the same as to-day, ended with a black eye or other bruises, and leeches were then employed as a relief. The Bible does not mention such an occurrence about Adam and Eve or their descendants, but states in Proverbs XXX, 15: "The leech hath two daughters, crying Give, Give."

In old Indian medicine leeches were used, according to Susruta in his "Ayur-Weda," supposed to date back to 1300 B. C. The followers of Hippocrates (about 400 B. C.), the father of the Greek school of medicine, did not employ leeches, as they preferred blood-letting. Plinius (about 50 A. D.), the celebrated Roman historian, in his "Historia Naturalis" describes the uses of leeches for withdrawing

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