

A NEW FEATURE IN IODIZED OILS¹

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SINCE the introduction of iodized oil in therapy by Sicard and Forestier (1), its usefulness has been established, confirmed, and generally accepted by the medical profession for roentgen diagnosis and iodine medication. Sicard and Forestier produced an iodized poppy seed oil. Other iodized oils which are also available on the market to-day are iodized sesame oil and iodized rapeseed oil. Subsequently, brominated oils were also prepared. In all these halogenated oils, the unsaturated fatty acids of the oil are chemically combined with only one halogen, such as iodine, or bromine.

In 1897, E. Merck, in Darmstadt (2), patented a method for making fats containing small amounts of iodine. In this patent the fact was emphasized that the presence of chlorine caused a darkening of the oil, and decomposition occurred in a very short time. If, however, quantities of the reagents forming iodine and chlorine in amounts below the theoretic one are used, then there were obtained stable oils containing iodine in amounts of 2, 5, 10, or 15 per cent and chlorine in very small amounts. In a patent (3) assigned to Merck and Company in 1909, Seifert points out that, up to that time, the following facts were known:

1. Complete treatment of fats with "chlor-iodine" yields "chloriodine" fats not stable and not suitable for medicinal use.

2. Complete treatment of fats with hydriodic acid or with iodine and reducing agents yields iodine fats not stable and not suitable for medicinal use.

3. Incomplete treatment of fats with chloriodine yields stable chloriodine fats suitable for medicinal use.

4. Incomplete treatment of fats with hydriodic acid or with iodine and reducing agents yields stable iodine fats fit for medicinal use. However, the incomplete treatment yields only fats or oils with a low percentage of iodine and a very low chlorine content.

In 1928 two physicians (4) prepared iodine trichloride by passing chlorine gas over iodine. This they then dissolved in water and shook it with corn oil. This oil was used for their sinus work. They did not mention the iodine content of the oil nor were they aware of the fact that the chlorine was most probably also combined chemically with the oil.

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This was the status of the attempts to prepare fatty oil containing both chlorine and iodine when the problem was taken up in our research laboratories in 1929. In selecting the oil for our study, we were guided by a high iodine value, low specific gravity, low content of the free fatty acids. We also considered (5) that the unsaturated fatty acids, especially linoleic acid, of the oil are highly responsible for the irritating action of iodized oils. Poppy seed oil contains about 65 per cent of linoleic acid, while peanut oil contains only from 21.6 to 24.7 per cent. From these considerations we finally decided to use peanut oil. Peanut oil, called *Oleum Arachis*, also, is composed chemically of the glyceryl esters of the following fatty acids: oleic, linoleic, palmitic, stearic, and arachidic. In addition, peanut oil contains in small amounts high melting fatty acids such as the normal eicosanic, docosanic, and tetracosanic acids described by Taylor (6) and Yantzen and Tiedke (7). These last investigators doubt very much the presence of

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Fig. 1. Study of antrum, iodochlorol injection. (Courtesy George D. Wolf, M.D., New York.)

lignoceric and isobehenic acids in peanut oil. This unique chemical composition is another reason why peanut oil was selected. No other vegetable oil offers such a wide variety of fatty acids as those contained in peanut oil, some of them being entirely specific for peanut oil only.

From a glance at Table II one will notice that peanut oil has a low specific gravity, a fairly high saponification value, and iodine value. The content of the free fatty acids in the native oils is very low. These physical properties make peanut oil a very suitable vegetable oil for the purpose of making halogenated oils.

We succeeded in introducing iodine and chlorine in peanut oil in such a fashion that the oil was saturated with halogens accord-

ing to the iodine number of peanut oil. One important feature in the manufacture of this halogenated oil is the fact that the free fatty acids are removed before and after halogenation, which removes the irritating properties and also affords remarkable stability to the halogenated oil.

This iodized and chlorinated oil, which is otherwise known as iodochlorol, contains about 27.5 per cent of iodine and 7.5 per cent of chlorine, so that the total content of halogen amounted to about 35 per cent. The action of chlorine and iodine is complementary and whether or not this results in a better shadow than produced by an oil containing iodine alone remains to be established. The halogenated oil so obtained has a brilliant yellow color, a specific gravity of 1.290 at 15.5° C., and a relative viscosity of 103, while the original peanut oil has a relative viscosity of 5.24.

ESTERS OF THIS HALOGENATED OIL

For many purposes, in fact for most purposes, this high viscosity of the halogenated oil is very desirable, but for some purposes, as in urologic work, a very low viscosity is desired. To accomplish this, we prepared the ethyl esters of peanut oil by esterifying the peanut oil with ethyl alcohol, introducing iodine and chlorine, which resulted in the formation of iodized and chlorinated esters of peanut oil, containing about 25 per cent of iodine and 7 per cent of chlorine. These esters are much more limpid than the oil, having a viscosity of 4.24, a specific

TABLE I.—FATTY ACID CONTENT OF TWO KINDS OF PEANUT OIL

Oils from	Oleic acid per cent	Linoleic acid per cent	Palmitic acid per cent	Stearic acid per cent	Arachidic acid per cent
Spanish nuts	52.1	24.7	8.2	6.2	4.0
Virginia nuts	60.6	21.6	6.3	4.9	3.3

TABLE II.—PHYSICAL CONTENTS OF PEANUT OILS

	Oil from Vir- ginia nuts	Oil from Spanish nuts	Oil from African nuts	Commercial oil
Specific gravity at 15° C.	0.917	0.9175	0.911	0.9209
Saponification value	192.5	190.68	194.0	192.1
Iodine value	91.75	94.17	85.6	98.4
Hehner value	94.87	95.31		
Free fatty acids, as oleic acid	0.55	0.79	0.62	6.2
Cold test	+3°	+3°	+2°	+10°
Melting point of fatty acids	29°	34°	30°	28°
Solidifying point	27.5°	32.5°	29.0°	25°

TABLE III.—VARIOUS CONSTANTS OF VEGETABLE OILS AND THEIR HALOGENATED PRODUCTS

Name of oil	Specific gravity at 15.5° C.	Relative viscosity*	Iodine number	Saponification number	Acid value
Peanut oil	0.917 - 0.9209	5.24	83 - 103	189 - 196	0.5 - 5.0
Iodochlorol (iodized and chlorinated pea- nut oil)	1.290	103.01			
Iodized ethyl esters of peanut oil	1.21	4.24			
Rapeseed oil	0.9133 - 0.9168		94 - 106	167.7 - 179	1.4 - 13.2
Iodized rapeseed oil	1.289	30.21			
Poppy seed oil	0.9255 - 0.9268		132.6 - 136	190.1 - 197	0.7 - 11.0
Iodized poppy seed oil 40 per cent	1.340 - 1.350 at 20° C.	63.17			
Sesame oil	0.9203 - 0.9237		103 - 115	188 - 197	0.23
Iodized sesame oil 40 per cent	1.370 - 1.372				
Olive oil	0.9150 - 0.9180		75 - 88	185 - 196	1.9 - 50.0
Brominized olive oil 33 per cent	1.16	3.77			

*The term "relative viscosity" used here was taken to = $\frac{\text{time} \times \text{density (oil)}}{\text{time} \times \text{density (water)}}$

gravity of 1.21, and are stable to light and heat.

Table III shows the various physical properties of some vegetable oils and their halogenated products.

From this table it is seen that iodized and chlorinated peanut oil has the highest relative viscosity of all halogenated oils, while the iodized and chlorinated esters of peanut oil have, with the exception of brominized olive oil, the lowest viscosity. Even the iodized and chlorinated peanut oil is suffi-

ciently heat stable to be sterilized by pasteurization.

TOXICITY

Iodized and chlorinated peanut oil is non-irritating due to the fact that the iodine and the chlorine are firmly held in organic combination. The chlorine is just as firmly combined chemically as the iodine, so that no possible irritation could occur due to the presence of chlorine. The halogenated oil is also non-irritating due to the fact that the



Fig. 2. Study of antrum, iodochlorol injection. (Courtesy Millard F. Arbuckle, M.D., St. Louis.)



Fig. 3. Monolateral bronchiectasis, iodochlorol by passive aspiration. (Courtesy Hugo O. Deuss, M.D., Chicago.)

peanut oil is highly refined before and after it is subjected to iodization and chlorination. It is, as has been established by animal experiments in our laboratories, of low toxicity and, therefore, well tolerated in large amounts. The esters of this halogenated peanut oil are likewise non-irritating and of low toxicity.

USES OF IODIZED OILS

In iodine medication, in cases in which large amounts of iodine are indicated, iodized and chlorinated peanut oil may be given in large doses, one to two teaspoonfuls, without producing any ill effects, such as iodism, etc. Iodized oils produce in general the same systemic effects as ordinary iodides, but their iodine is more slowly absorbed and excreted and they are more persistently retained in the tissues, especially in tissues rich in lipoids. The iodized oils generally pass the stomach unchanged and are saponified and absorbed in the small intestine. They are then deposited for the most part in lipid tissues, in which they are gradually oxidized, yielding inorganic iodide, which is given off to the blood.

When a gradual long-sustained iodide action is desired, iodized oils have therapeutic advantages over ordinary iodides. Larger doses may be given than is the case in inorganic iodides without producing iodism.

In sinuses, recent investigators highly recommend the use of iodized oils for diagnosis (8, 9), pointing out that they can be injected into the various sinuses without harmful effects. Iodized peanut oil is particularly suitable in this field, because its viscosity is high and does not have to be diluted with heavy petrolatum or olive oil as is the case with other iodized oils.

Wolf (10) praises iodized oil for the study of antra and recommends its use in large institutions as a routine procedure. In the usual displacement technic, Proetz (11) obtained very satisfactory results by the use of iodized oil.

In our own researches with our iodized and chlorinated peanut oil (iodochlorol) in sinuses, X-ray plates of deep shadow, clearness, and sharpness were obtained, unexcelled by those obtained with any other contrast medium.

Figures 1 and 2 are illustrations of the study of antra by means of our iodized and chlorinated peanut oil.

In bronchography through the use of iodized oils, considerable progress has been made within recent years. The non-irritating properties of iodochlorol make it well adapted for this use. Wood (12) recommended the oral administration of iodized oil as an aid to the differential diagnosis of upper lobe bronchiectasis and pulmonary tuberculosis.

After several injections of iodized oil by aspiration into the lungs, Singer (13) reports satisfactory results in a case of streptothricosis. Stiehm (14) gives complete credit to the insufflation of iodized oil for successful treatment of bronchiectasis. Hygienic living, postural drainage, rest, and the systemic effect from the iodine content of the iodized oil are all possible factors. Case histories show that patients treated with iodized oils do better than those without this treatment. Eschbach (15) reports on a pulmonary gangrene cured by tracheal injection of iodized oil. Surgical intervention in such cases is difficult and dangerous. Eschbach recommends the use of iodized oil before operation is performed. According to Iglauer (16), endo-



Fig. 4. Study of bilateral bronchiectasis, iodochlorol by passive aspiration. (Courtesy Hugo O. Deuss, M.D., Chicago.)



Fig. 5. Exploration of fallopian tubes, iodochlorol injection. (Courtesy Robert A. Arens, M.D., Chicago.)



Fig. 6. Normal retrograde pyelogram, iodochlorol emulsion. (Courtesy Earl Ewert, M.D., Chicago.)

bronchial injection is well borne by the patient, no disturbing effects being encountered. He recommends slow injection with the use of a special intubation instrument. Injection of the oil is contra-indicated in febrile or cachectic patients and in those with cardiac decompensation. Expectoration is usually increased for a few days after the introduction of the oil, a considerable portion being thus ejected. The remainder is eliminated by absorption.

Singer (17) describes the introduction of the iodized oil into the lungs by pulling the tongue out as far as possible and introducing the iodized oil with a straight cannula and a 20 c.c. syringe. Perfect films of the bronchiectatic cavities of the lungs were obtained in 25 cases. Archibald (18) pointed out the fact that iodized oils are contra-indicated in cases of tuberculosis and infections of the upper respiratory tract. In an

interesting study, Pinkerton (19) pointed out that iodized vegetable oils do not produce any reaction and do not appear to injure the lungs in any way. Their removal from the lungs seems to be accomplished entirely by expectoration. *Free fatty acids* in the oil produce necrosis in the lung tissue. The degree of drainage and resulting fibrosis produced by an oil in the lungs depends largely on the amount of free fatty acids originally present and on the rapidity with which hydrolysis progresses. The almost complete lack of reaction to neutral vegetable oil in the lung is probably due to the absence of enzymes capable of hydrolysing the oil.

A unique study was made by Zalewski (20), who used Finikoff's method to increase the defensive mechanism of the organism by stimulating the lipolytic and the proteolytic power of the blood. This was accomplished by intramuscular injections of iodized oil and by the peroral administration of calcium salts. Zalewski reported excellent and lasting results with this method in osteo-articular tuberculosis, tuberculosis of the epididymis, and lymph node tuberculosis.

Faulkner (21) studied the uses of iodized oil in pulmonary suppuration and found that intrabroncheal injections of iodized oils permit a study of "internal drainage." Internal drainage is the spilling of pus from a diseased bronchus to the neighboring bronchi of either lung.

Soresi (22) has facilitated greatly the use of iodized oil for intratracheal injection by working out a simplified technic. He injects the iodized oil through a syringe (the oil being kept lukewarm), inserting the syringe into a special cannula tongue depressor. He anesthetizes the organs thoroughly, which avoids dripping of oil into the esophagus even if the patient moves the head.

In our own investigations, we have found iodized and chlorinated peanut oil (iodochlorol) very suitable for the study of monolateral and bilateral bronchiectasis, particularly if three parts of iodochlorol are mixed with one part of the iodized and chlorinated ethyl esters of peanut oil. The results obtained are shown in Figures 3 and 4.

In gynecology, considerable work has recently been done on the exploration of the fallopian tubes and the uterus for sterility investigation. The leading researches of Stein and Arens (23) have opened this field, making it accessible to almost every obstetrician and gynecologist. They devised a new radiographic table for pelvic radiography with iodized oil and pneumoperitoneum, combined the method of pneumoperitoneum with the one of iodized oil instillation (24) and obtained very satisfactory results. According to Rubin and Bendick (25), iodized oils should not be injected into the uterus without first proving, by peruterine carbon dioxide gas insufflation, that the fallopian tubes are definitely non-patent. Witwer, Cushman, and Leucutia (26) assert that hysterosalpingography by means of iodized oil is a safe and simple procedure. In a series of 152 cases, the authors observed only one accident, that of a ruptured tube which did not lead to any ill effects. The method is of great diagnostic value in developmental anomalies of the genital organs, in tubal conditions leading to sterility, in certain carefully selected cases of pregnancy, and in uterine tumors. The method is contra-indicated in recent hemorrhagic inflammatory conditions that are not completely quiescent, active infections or malignant growths involving the cervix, previous intra-uterine intervention, uterine gestation in which a therapeutic abortion is not desired, infected cervical or uterine polyps, and fever. In certain instances, the injection of iodized oil is of direct therapeutic value.

Lash (27) successfully used iodized oil in

cases of uterus bicornis, bilateral salpingitis, and pelvic peritonitis. The function of the tubes was not disturbed by the iodized oil as the patient delivered a full-term child one year after injection. Lash, however, believes that, in the presence of infections in the female generative tract, the use of iodized oils is contra-indicated, as they have no antiseptic properties.

That our own studies have given very satisfactory results with iodochlorol for the exploration of the fallopian tubes can be seen from Figure 5, obtained with our iodochlorol.

USE OF IODIZED AND CHLORINATED ESTERS OF PEANUT OIL

While intravenous pyelography has certain theoretic values, in actual practice the main reliance is still based upon retrograde pyelograms. A good pyelographic medium must have the following properties to be of service to urologists:

1. It should give a good shadow.
2. It should have a low viscosity and should be miscible with water in all proportions.
3. It should be of low toxicity and free from all irritation.

Our research laboratories have succeeded in developing such a medium, called iodochlorol emulsion (Searle). The active ingredient in this emulsion is the iodized and chlorinated ethyl esters of peanut oil, containing about 25 per cent of iodine and about 7 per cent of chlorine. It has a specific gravity of from 1.19 to 1.22 at 25° Centigrade. It has a relative viscosity of 4.2. This extremely low viscosity makes the iodized esters very suitable for pyelographic work, as the emulsion has a still lower viscosity. The iodized ethyl esters of peanut oil are mixed with a small amount of mineral oil and emulsified with 10 per cent potassium oleate. The emulsion also contains 0.5 per cent benzyl alcohol.

The use of iodized oil in emulsion form was first studied by Neuswanger (28, 29), who, as early as 1926, reported favorably on its use as a pyelographic medium. Langer (30), in Germany, obtained excellent pyelograms by the use of emulsified iodized oil. No evidence of irritation or other injurious complications were obtained and it was borne without reaction of any kind. Behrenroth (31) used the iodized oil in non-emulsified form and, while he at first reported favorable results, he encountered difficulties because he used the oil as such and not in emulsified water-miscible form.

In our own researches we found that the iodochlorol emulsion gave excellent pyelograms of great density and sharpness. The emulsion was well tolerated and no irritation or reactions of any kind were obtained. The emulsion was readily eliminated a few hours after the injection into the catheter. Pyelograms were obtained with this iodochlorol emulsion, Figure 6 being typical of all of them.

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SUMMARY

1. A new iodized peanut oil, containing approximately 27.5 per cent of iodine and 7.5 per cent of chlorine, and ethyl esters of the oil have been described.

2. Besides the high radiopacity due to the presence of two halogens, they possess the following properties:

(A) In sinus diagnosis, the high viscosity of the oil is an advantage.

(B) In bronchography, the non-irritating qualities of this oil and the viscosity, made controllable by adding the esters to the oil, make it particularly valuable.

(C) In gynecology, in recent studies of the exploration of the fallopian tubes, it has been found suitable.

(D) In pyelography, an emulsion of the esters was shown to have ideal properties for retrograde pyelograms.

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Viosterol Found Beneficial to Radium-poisoning Victims.—Almost simultaneously with the news of the twentieth death from radium poisoning among the unfortunate watch factory workers, comes the announcement of a promising method of treating the condition. Viosterol, now often given children in place of cod liver oil to prevent or cure rickets, has benefited a number of victims of radium poisoning, Dr. Frederick B. Flinn, of Columbia University, has reported to the American Medical Association. Dr. Flinn does not consider that he has a cure for the condition, but merely reports a method of treatment that has given promising results.

"Our experience so far suggests a method of treatment that will eliminate radium salts from the organism as well as improve the condition of the bones if continued for sufficient time," he stated. "It is a matter of months and not days. Care should be taken that fresh preparations are used," he cautioned.

Most conspicuous among radium-poisoning victims were the dial painters in the watch factory who used to put their radium-paint brushes in their mouths to point them. In this way radium entered their bodies and in about one-fifth of the cases the radium was deposited in the bones instead of being eliminated. While the amounts of radium ab-

sorbed in this way were small, the activity of radium is so great that these small amounts were sufficient to destroy bones and tissues and to cause fatal illness.

How to get the radium out of the body before it had caused irreparable destruction was the problem which Dr. Flinn and other scientists attempted to solve. Because radium is related to calcium, it was supposed that any treatment that would affect calcium might have a similar action on the radium deposits, Dr. Flinn explained. So he first tried treatment with an extract of the parathyroid glands, because these glands are thought to regulate the calcium of the body. Parathyroid treatment had been moderately successful, when Dr. Flinn suggested the use of viosterol. Vitamin D, calcium utilization in the body, bone formation, and the parathyroid glands are all linked together, so viosterol, which is a potent source of Vitamin D, was a logical selection.

The results of this treatment in eight cases have been good. In two cases, radium was completely eliminated from the body; in the other six, the amount of radium was materially reduced. Improvement in general health, such as freedom from pain, gain in weight, and improved condition of the blood, followed the treatment. In most of the patients the destruction of bone was checked.—*Science Service.*