THE PHARMACY OF OXYPINENE.

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Oxypinene or Pinene Ozonide is so little known to pharmacists, that it may be well first to consider what is known about its composition chemically, and its use therapeutically, before taking up briefly the pharmacy of this most interesting substance.

In the May, 1915, issue of the American Journal of Pharmacy appears an article on Oxy-Pinenes by J. Emile Blomén, A. M., Ph. D.

He says: "Nowhere in nature can be found a more marvelous 'dead' organic substance than this one (Terebinthina) which, like a living being, inhales oxygen from the air and, transforming it, gives it off in another form."

We know that the pinene is the substance that "inhales" oxygen forming oxides which are given off as oxygen. If in place of oxygen, ozone is placed in contact with pinene, under certain conditions it will be "inhaled" and ozonides will be formed which will give off oxygen in a nascent form.

"When ozonides of pinene come in contact with moisture, they are decomposed, forming hydrogen peroxide and oxygen compounds or pinene. On prolonged standing or by heat, intermolecular or auto-oxidation will take place, resulting in the higher oxidation products of pinene, pinonic acid, etc."

Oxypinene or ozonide of pinene $C_{10}H_{16}O_8$ is a heavy viscid liquid of a light yellow or lemon color, having an agreeable turpentine odor and taste. It is soluble in some fixed oils, most volatile oils, chloroform, ether, alcohol, etc. Dr. Blomén promises to give a history of the uses of the oxypinenes and we hope he will include more of the chemistry also.

Oxypinene is prepared by exposing the vapor of pinene to a current of ozonized air, prepared by the action upon dry air of a high tension electrical discharge. An addition occurs between the pinene and oxygen resulting in the production of a dense white vapor (Oxypinene)."

This description is taken from the very able article by Dr. Bertram H. Waters, M. A., M. D., published in the Medical Record, February 13th, 1915. He says further, that in making oxypinene, only pure pinene and ozonized air should be used.

From clinical observation, Dr. Waters concludes that, "Oxypinene is useful in subacute and chronic affections of the respiratory system and is indicated as a mild stimulant to the mucous membranes and other tissues. When brought in contact with infected surfaces, it inhibits the growth of certain pathogenic microorganisms, and, by its pathogenic property, increases the circulation in the infected area, thus promoting the destruction of such organisms by phagocytosis."

It is reasonably certain that the treatment of wounds with old turpentine, found by surgeons during the Civil War so useful against gangrene, owed its efficacy to oxypinene in a crude state.

We have been informed that this same old-fashioned treatment is now in use in the German army.

^{*} Read at meeting of Pennsylvania Pharmaceutical Association, 1915.

Ozonide of pinene, or Oxypinene as Dr. Waters calls it, is probably the most concentrated form of the valuable parts of "old turpentine" and therefore, should be particularly valuable in treating wounds, ulcers, etc.

In making pharmaceutical preparations of oxypinene, it must be remembered that decomposition with formation of hydrogen peroxide and pinene compounds takes place when water is used, and unless this is desirable, water is to be avoided.

Also all oxygen compounds loosely combined are more or less dangerous to handle unless care be used. High temperatures are to be avoided or exposure to air for any length of time. For instance, in making an ointment of oxypinene, such bases as ointment of rose water, hydrous wool-fat, etc., are to be avoided on account of the water they contain. Also the ingredients should not be melted together or if they are, the oxypinene should not be added until they are cold as any excess of heat will cause "the intermolecular or auto-oxidation" mentioned by Dr. Blomén in his paper above referred to.

In making suppositories, the heat required to melt a cacao butter base is so little that it need not be considered; but, as oxypinene does not combine well with cacao butter and as there are so many qualities of cacao butter on the market, and as there is another substance superior in every way and inferior in no respect, we need not hesitate to mention Stearate from Cocoanut Oil as being the best vehicle.

About one percent of oxypinene in rectal and vaginal suppositories has given excellent results clinically.

For use in treating eczema, skin affections, hemorrhoids, etc., a very efficient compound ointment has been in use for some time in an experimental way clinically. It is made by using a base composed of cocoanut oil and petroleum, talcum, starch, and zinc oxide, resorcinol and oxypinene.

Considerable experimental work has been done in an endeavor to produce a powder for dusting wounds and for internal administration in enteric pill or capsule form. It is believed that diatomaceous earth produces the best results.

A powder made by incorporating one part of oxypinene with two parts of kieselguhr is satisfactory. Such powder should be kept in sealed containers, for not only is oxypinene in this form liable to undergo auto-oxidation, but the kieselguhr seems to have a catalytic action, as the powder gains considerable in weight when exposed to air for a comparatively short time. One would suppose this extra weight to be water from moisture in the air, but careful chemical examinations has proven it to be oxygen. It is therefore a fact that through the catalytic action of kieselguhr, this powder absorbs oxygen from the air, which makes it a more valuable dressing for wounds than it would otherwise be.

Dr. Waters has found Oxypinene Vapor to be a useful form with which to treat disease. It is not a gas but a vapor and is made up of such finely divided particles, that it floats about in the air, resembling smoke. It is produced by bringing pinene $(C_{10}H_{16})$ vapor and ozonized air into intimate contact in a mixing chamber.

Pinene Vapor is produced by allowing a current of dry air to pass over the surface of volatile pinene. The ozone is made by silent electrical discharges in purified air. In order to avoid the production of nitrates and gaseous peroxides, the air which is used in generating oxypinene must first be freed from moisture; this also allows a higher degree of saturation with the volatile pinene.

Oxypinene Vapor may be inhaled mixed with the air of a room or directly from the generator by means of a suitable mask. For the treatment of superficial lesions on the surface of the body, it is used by allowing it to flow directly upon the affected surface.

When inhaled oxypinene acts as a stimulating expectorant. When applied to the skin it acts as an antiseptic stimulant.

SUMMARIZING.

Oxypinene is an ozonide of pinene, a chemical compound consisting of one or two molecules of ozone (O_3) linked to one molecule of pinene $(C_{10}H_{16})$ the active and chief constituent of oil of turpentine.

It is produced in two forms, a vapor and a pale yellow liquid of honey-like consistency.

On contact with moisture it breaks down into hydrogen peroxide, oxides, aldehydes, and ketones or pinene.

Exposed to high temperature auto-oxidation takes place.

It is useful in treatment of tubercular affections, wounds, ulcers, diseases of the mucous membranes, eczemas, hemorrhoids, etc.

It is an expectorant, stimulant and oxidizing agent.

Mixed with diatomaceous earth, one part to two parts, it makes a suitable powder for dressing ulcers, old wounds, etc.

Made into suppositories with stearate from cocoanut oil, about one percent strength, it is very useful in treating diseases of the membranes when a stimulating, mild antiseptic is required.

In a compound ointment combining astringent and drying properties with its antiseptic and stimulating effect, it is useful in eczemas and in certain cases of hemorrhoids.

The vapor may be inhaled from a generator or indirectly mixed with air.

The liquid may be applied to wounds in its strongest form.

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J. W. ENGLAND,

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^{*} Read at meeting of Pennsylvania Pharmaceutical Association, June, 1915.