The Fungicidal Activity of Certain Volatile Oils and Stearoptens

THEIR COMPARATIVE TOXICITY ON A PATHO-GENIC YEASTLIKE ORGANISM: REPORT OF CLINICAL UTILIZATION IN RELATED INFECTIONS

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The fruit packing plants of the Pacific Northwest have been troubled for several years with a dermatosis developing among employees engaged in preparing the fruit for canning. The lesion has been referred to by those affected as a "fruit poisoning." It has been treated without much success by a great variety of means, chiefly by the antiseptics commonly utilized in treating bacterial infections.

A person with an interdigital lesion that originated while employed in one of the fruit packing plants came to our attention a few months ago. The infection referred to had persisted for several months in spite of the use of various prescribed standard antiscptics. Scrapings from the lesion revealed budding spore forms with mycelium attached, which we believed to be responsible for the inflammatory reaction. A 10 per cent. alcoholic solution of the oil of cinnamon was painted over the inflamed area. Rapid improvement in the appearance of the lesion, progressing to healing, followed the application of the cinnamon solution. It might be remarked that the oil of cinnamon was tried because of its efficacious use against mold growth in such preparations as the infusion of digitalis and in mistura cretae.

The canning plant in which the lesion referred to had originated was visited during the next pear canning

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season. The infection known as fruit poisoning had been particularly severe during the time pears were handled, in previous years. Many cases of infection, similar in gross pathology and in cultural findings to the one we had originally seen, were found. These lesions healed rapidly with the use of spirit of cinnamon. We understand from the manager of the plant and the chemist employed that the directed use of cinnamon water was efficacious as a prophylactic measure in preventing a greater number of infections.

A report of a dermatologic study of the lesion produced by this pathogenic yeastlike organism has recently been made by Kingery and Thienes. Experimental inoculations in man and animals resulted in lesions similar to those found in the fruit workers.

The favorable action of oil of cinnamon on the original and experimental lesions led to an investigation of the comparative toxicities of several volatile oils and stearoptens on cultures of the pathogenic yeast responsible for the infections.

EXPERIMENTAL METHODS

It was considered advisable to avoid the complicating action of any solvent of the volatile oils other than water. The preparation of official aquae of the volatile oils is directed by the United States Pharmacopeia. While differences in the water solubilities of the several volatile oils considered must exist, the aquae, as saturated aqueous solutions, are usually considered to be between 0.1 and 0.2 per cent. strength. Greater differences in strength exist between the aquae of the stearoptens included in this study. Comparison of fungicidal power was made with a 1 per cent. aqueous solution of phenol (carbolic acid).

Twenty-four hour cultures of the yeast in meat-extract broth were exposed to aquae of several volatile oils and stearoptens. At definite time intervals, subcultures were made into meat-extract broth and incubated at 35 C., previously found to be the optimal temperature for this organism. Following twenty-four hours' incubation of the subcultures, streak inoculations were made on plates of Sabouraud's medium. The results of these cultural tests are shown in the accompanying table.

^{1.} Kingery, L. B., and Thienes, C. H.: Mycotic Paronychia and Dermatitis: Hitherto Undescribed Condition Apparently Peculiar to Fruit Canners, Arch. Dermat. & Syph. 11: 186-202 (Feb.) 1925.

Considerable variation has been found in the fungicidal powers of the oils studied on the yeastlike organism responsible for the so-called fruit poisoning. For example, the yeast grows just about as luxuriantly in the aqua of oil of lemon as it does in the broth medium. Thymol is about the least soluble in water of all the stearoptens and oils studied so far. The aqua thymolis destroys the yeast in sixty seconds or less. Phenol in 1 per cent. solution requires sixty minutes to kill the organism. The most efficient volatile oils are cinnamon and cloves, requiring approximately thirty and ninety minutes, respectively, to prevent growth of the yeast. The majority of the oils, camphor and menthol, in

Comparative Fungicidal Power of Certain Volatile Oils and Stearoptens on a Pathogenic Yeast

		Minutes Required to Destroy Pathogenic Yeast										24
Aquae	1	10	20	30		50			80	90	100	Hrs.
Thymol	-		.,				٠.	• •		٠.		
Clove	Ŧ	7	+	Ŧ	+	+	7:	+	+	±	_	::
Menthol Peppermint	#	#	+	‡	+	±	‡	+	+	+	+	_
Camphor	÷	+	+	÷	÷	+	+	÷	+	+	+	-
Methyl salicylate Turpentine	Ŧ	1	+	‡	#	+	1	‡	+	+	+	
Eucalyptus Toluene	<u>+</u>	±	+	±	+	+	İ	+	<u>+</u>	+	±	_
Lemon	Ŧ	Ŧ	Ŧ	Ŧ	Ŧ	Ŧ	Ŧ	Ŧ	Ŧ	Ŧ	Ŧ	+
Phenol, 1 per cent	+	+	+	+	+	+	_			• •		٠.

 $[\]pm$ indicates growth; $\pm,$ no growth; $\pm,$ feeble growth in minority of cultures; majority sterile.

saturated aqueous solution did not apparently inhibit the growth of the yeast in 100 minutes.

CLINICAL USE

A mixed spirit composed of 5 per cent, thymol and 2 per cent, cinnamon, painted on sites of infection found on employees in the canning plant previously mentioned, was found to cause a speedy relief of discomfort and promotion of healing.

The efficient action of thymol and cinnamon oil in the treatment of the moniliosis of the fruit handlers has led to a trial of its service in several infections due to different types of fungi. The results briefly have been as follows:

Several patients with epidermophyton infection between the toes and on the soles of the feet have had prompt relief and a resulting healthy skin from the use of the thymol and cinnamon mixture referred to. One student stated that his infection had started as "trenchfoot" disease while in service overseas. Several of those with this type of infection had used Whitfield's ointment and other remedies with but partial relief.

Hand infections caused by a sarcinae type of organism, producing minute, coalescing vesicles, particularly when the finger surfaces were in apposition, showed improvement in less than twenty-four hours following the application of the spirit, and disappeared in a few days. Three additional cases of sarcinae infection in other parts of the body, each one of long standing, yielded promptly to the use of thymol and cinnamon solution. Two of the three patients mentioned stated that they had used numerous ointments and lotions, and had received actinotherapy.

Two persons with pulmonary mycosis have been given thymol in capsule, and thymol with cinnamon oil by inhalation of nebulized solution in liquid petrolatum. One patient exhibiting symptoms of steadily increasing pulmonary involvement previous to taking the drugs mentioned has shown constant pulmonary and general improvement following a period of about six weeks in an apparently stationary condition. The organism believed responsible, apparently Aspergillus niger, is steadily disappearing from the sputum. In the second case of pulmonary infection referred to, the drugs have been given for less than four weeks, and there has been no change to date.

A low-grade acute infection of the forearm, producing an amber colored discharge, yielded a budding yeast producing a yellow pigment on Sabouraud's medium. Pain and itching stopped in a few hours following the application of a wet dressing of the thymol and cin-

namon solution. Healing occurred promptly.

A patient with actinomycosis of the face and neck, failing to improve under deep roentgen-ray treatment, was given large doses of sodium iodid with resulting improvement. The improvement under iodid apparently progressively lessening or at a standstill with dosage exceeding 40 gm. daily, further administration of the salt was stopped, and thymol given twice a week in doses increasing from 0.5 gm. to 1.5 gm. Definite improvement in the appearance of the lesions followed the use of thymol, and the patient left the hospital

apparently cured after two months' use of thymol, without other medication during that time. He is now under observation in the outpatient department without evidence of recurrence to date.

It is impossible to state what part the thymol played in the improvement of the case of actinomycosis. Further trial in such cases will establish its relative merit.

The infections mentioned have been encountered in a limited number of persons, without particular search, giving us the impression that infections of this type may be more common than is generally considered to be the case.

The volatile oils are known to have a particular toxicity toward molds and yeastlike organisms. They have apparently not received the attention in clinical application that their activity warrants. In a report on studies in the chemotherapy of fungus infections,² thirty medicinal agents are mentioned without the volatile oils being included. One gains the impression from the recent literature on mycotic infections that the volatile oils are not made use of to any noticeable extent, in treatment,

SUMMARY

Thymol, oil of cinnamon and oil of clove have been found particularly efficacious in destroying a pathogenic yeastlike organism responsible for an occupational dermatitis

The drugs mentioned have been found equally valuable in causing an immediate improvement progressing to healing of infections apparently due to fungoid organisms of several types.

The results reported warrant further trial of the volatile oils and stearoptens in infections due to fungoid organisms.

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^{2.} Schamberg, J. F., and Kolmer, J. A.: Studies in the Chemotherapy of Fungus Infections, I, The Fungistatic and Fungicidal Activity of Various Dyes and Medicaments, Arch. Dermat. & Syph. 6:746-756 (Dec.) 1922.