o-amphiphiles are located at the periphery of the micelle with the lipophilic tail of the molecule within the hydrocarbon nucleus and the hydrophilic carboxylic acid group protruding into the palisade layer.

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Toxicities of Peppermint and *Pycnanthemun albescens* Oils, fam. *Labiateae*

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The oral LD_{50} of peppermint oil U.S.P. in fasted Wistar male rats using death after 24 hr. as the end point was found to be 4441 ± 653 mg./Kg. After 48 hr., the oral LD_{50} was 2426 ± 329 mg./Kg. The intraperitoneal LD_{50} of peppermint oil U.S.P. in Wistar male rats similarly after 24 hr. was determined to be 819 ± 126 mg./Kg. This latter was compared with a similar volatile oil, *Pycnanthemum albescens*. It was found to have an intraperitoneal LD_{50} in male Wistar rats similarly after 24 hr. of 1383 ± 172 mg./Kg., which was only approximately 60 per cent as toxic as peppermint oil U.S.P. The oral LD_{50} of *P. albescens* oil in fasted Wistar male rats after 24 hr. was 5309 ± 818 mg./Kg. After 48 hr., the oral LD_{50} was 3147 ± 362 mg./Kg.

PEPPERMINT oil enjoys very popular use as a flavoring agent and as an occasionally used carminative and anticolic aid. The list of preparations in which peppermint oil is used is extensive.

The U.S.P. XVI defines peppermint oil as containing not less than 5% of esters, calculated as menthyl acetate, and not less than 50% of total menthol, free and as esters.

The toxicity of peppermint oil is generally accepted as not being very great, and little reference is made to it. However, the LD of natural menthol, one of its major constituents, is stated to be 1000–2500 mg./Kg. in the rat administered subcutaneously in an oil vehicle (1).

Pycnanthemum albescens oil, having odor-blocking properties and antifungal activity, is composed of terpenes and apparently lacks any menthol content; but the exact chemical composition has not been determined. It is, however, a volatile oil, like peppermint oil from the family *Labiateae*.

It was, therefore, the purpose of this study to compare the oral and intraperitoneal toxicities between peppermint oil and *P. albescens* oil.

Received April 8, 1965, from the Department of Pharmacology, School of Pharmacy, Northeast Louisiana State College, Monroe.
Accepted for publication May 13, 1965.
The *Pycnanthemum albescens* oil for this study was provided by Dr. J. T. Goorley, Associate Professor of Pharmaceutical Chemistry, Northeast Louisiana State College, Monroe.
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EXPERIMENTAL

Male rats of the Wistar strain received 0.5, 1.0, and 2.0 ml./Kg. of peppermint oil intraperitoneally. The peppermint oil was U.S.P., double distilled [Penick and Co., New York, N. Y., control No. LCX-69, W84050 (sp. gr. 0.9021)].

Twenty animals were used at each dosage, and the LD_{50} after 24 hr. was determined using the Reed-Muench method (2). All animals in these studies were observed for a period of 30 days to include any possible latent effects.

Male rats, Wistar strain, in groups of 20 received, respectively, 0.5, 1.0, and 2.0 ml./Kg. of *P. albescens* oil intraperitoneally, and the LD_{50} after 24 hr. was calculated using the Reed-Muench method (2). The *P. albescens* oil was obtained by steam distillation from the stalks, leaves, and tops of the fresh plant (sp. gr. 0.9219).

Male rats of the Wistar strain were fasted at least 20 hr. but not longer than 24 hr., water given *ad libitum*. The animals were fasted in screen-bottom cages such that there was no access to feces or litter.

The fasted rats in groups of 20 received, respectively, 2.0, 4.0, and 8.0 ml./Kg. of peppermint oil orally by means of stomach intubation. The oral LD_{50} was calculated after both 24 and 48 hr. using the Reed-Muench method (2).

Additional fasted rats in groups of 20 received, respectively, 2.0, 4.0, and 8.0 ml./Kg. of *P. albescens*

TABLE I.—SUMMARY OF LD_{50} STUDIES OF PEPPERMINT AND *P. albescens* OILS ORALLY (IN FASTED ANIMALS) AND INTRAPERITONEALLY IN MALE WISTAR RATS

Dose, ml./Kg.	Dose, mg./Kg.	No. Dead/Total No. Treated After 24 hr.	After 48 hr.	LD_{50} Determined 24 hr.	48 hr.
				mg./Kg.	
		Peppermint Oil			
i.p. 0.5	451	5/20		819 ± 126	
1.0	902	10/20			
2.0	1804	19/20			
p.o. 2.0	1804	5/20	9/20	4441 ± 653	2426 ± 329
4.0	3608	5/20	14/20		
8.0	7217	18/20	20/20		
		P. albescens Oil			
i.p. 0.5	461	0/20		1383 ± 172	
1.0	922	5/20			
2.0	1844	15/20			
p.o. 2.0	1844	3/20	3/20	5309 ± 818	3147 ± 362
4.0	3688	8/20	15/20		
8.0	7376	13/20	20/20		

oil orally, and the LD_{50} was calculated after 24 and 48 hr. using the Reed-Muench method (2).

The dose in all animals was calculated on a ml./Kg. basis, and all the animals used were approximately 10 to 12 weeks of age, with average weight of approximately 200 Gm.

RESULTS

The animals receiving the peppermint oil intraperitoneally exhibited brief stimulation, followed by depression beginning in approximately 15 min.

Twitching, spastic convulsions, ataxia with hind limb paralysis, and abdominal contractions, very slowed respiration, and loss of righting reflex after 25 min. were all observed.

The results of the LD_{50} studies of peppermint oil intraperitoneally are listed in Table I.

The LD_{50} calculated from the results in Table I using death after 24 hr. as the end point was 819 ±126 mg./Kg.

The animals receiving the *P. albescens* oil intraperitoneally showed little or no stimulation but developed ataxia, spasms, and generalized intermittent to continuous clonic convulsions with slowed, deep respirations with loss of righting reflex similar to the animals receiving the peppermint oil. The hind limb paralysis and abdominal contractions were not present as with the peppermint oil-treated animals.

The results of the LD_{50} studies of the *P. albescens* oil intraperitoneally are listed in Table I.

The LD_{50} calculated from the results in Table I using death after 24 hr. as the end point was 1383 ±172 mg./Kg.

The fasted animals receiving the peppermint oil orally exhibited effects similar to those animals receiving peppermint oil intraperitoneally; however, the effects were much slower in appearing, taking 45 min. or longer to show the initial stimulation, twitching, and ataxia.

The results of the LD_{50} studies of peppermint oil orally in the fasted rats are listed in Table I. They were presented in two columns, after both 24 and 48 hr., as only with either of the oils administered orally did the additional 24-hr. period accumulate any large numbers of additional deaths.

The oral LD_{50} determined from the results in Table I using death after 24 hr. as the end point was 4441 ± 653 mg./Kg. and after 48 hr. was 2426 ± 329 mg./Kg.

Similarly, the fasted animals receiving the *P. albescens* oil orally were slower to manifest toxic symptomatology. The results are recorded in Table I.

The oral LD_{50} determined from the results using death after 24 hr. as the end point was 5309 ± 818 mg./Kg. and after 48 hr. was 3147 ± 362 mg./Kg.

The LD_{50} values determined are also listed in Table I.

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