TABLE I.
Fecal Fat and Nitrogen Excretion Before and After Cholecystectomy.
Means of 10-Day Tests on 8 Dogs.

Condition	Dietary fat g/day	Total fecal fat g/day		% free fatty acids		Fecal N, g/day	
		Mean	t-ratio*	Mean	t-ratio*	Mean	t-ratio*
Normal	53	2.43	—	68.6	—	.96	—
Cholecystectomy	53	1.96	.99	82.4	2.45†	1.09	2.06
"	80	2.44	.03	80.9	2.47†	.76	4.13‡

* Post-operative tests paired with normal tests.
† Significant at 5 per cent level of probability.
‡ Significant at 1 per cent level of probability.

unspecified amounts of fat and nitrogen over 48-hour test periods before and after cholecystectomy.[5]

Accordingly, in future experimental attempts to correct steatorrhea due to complete bile diversion, the manner of entry of bile preparations into the intestine, whether in continuous or intermittent doses, should not alter the results.

Clinically, these results further imply that bile salt replacement therapy and strict limitation of dietary fat are unnecessary as far as fat absorption is concerned in uncomplicated cases of cholecystectomy.

Conclusion. In 8 dogs studied both before and after operation, cholecystectomy produced no significant change in the daily excretion of fat or nitrogen in the feces.

[5] Balice, G., *Morgagni*, 1928, **70**, 835.

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In vitro Antibacterial Action of Extracts from Coptis Root.

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Recent investigations have demonstrated that higher plants are potential sources for antibiotics,[1] and, specifically, extracts of certain Chinese medicinal plants showed bacteriostatic action.[2] In view of the great potentialities of such a finding especially in relation to the study of the nature of action of some of the well known Chinese drugs, a detailed study of the root of *Coptis chinensis*, Franch, belonging to the family of Ranunculaceae,[3] has been made in the past 7 months. The present paper is a preliminary report of the antibiotic activity of the dilute alcohol extract of the coptis root against a number of microorganisms *in vitro*.

Method of Extraction. Samples of coptis root of Szechuan variety were obtained mostly from a well established and reputable Chinese pharmacy, Hsi Ho Nien Tang, Peiping, and some directly from Szechuan. The antibiotic activities of all the samples extracted with the method described below were found to be approximately the same. The macerated dried roots were placed in a large flask with 10 parts of 50% alcohol, and set aside at room temperature for 24 hours. At the end of this period the entire suspension was boiled for 30 minutes and filtered while hot through ordinary filter paper. The clear yellowish

[1] Benedict, R. G., and Langlyke, A. F., *Ann. Rev. Microbiol.*, 1947, **1**, 193.

[2] Hsü, C. L., *Nat. Med. J. China*, 1947, **33**, 75.

[3] Read, B. E., Chinese Medicinal Plants from Pen Ts'ao Kang Mu, 1936.

amber filtrate was then evaporated to dryness. The dried crude extract was yellowish brown in color and very bitter in taste. Its aqueous solution was used for various tests to be described.

Method of Assay. Series of 2-fold serial dilutions of the aqueous extract solution were made in 1% serum broth in small test tubes, and tubes of each series were seeded with one loopful of 18-hour broth culture of one of the many types of organisms to be tested. The tubes, after being shaken, were incubated at 37 C and readings were made after 24 hours incubation. The end point of bacteriostasis was taken as the highest dilution in which growth in the tubes was completely inhibited and subsequent cultures on blood agar plates still showed growth. Bactericidal power was determined by the absence of growth on subculture on blood agar plates.

Results. The effectiveness of the crude extract of the coptis root in inhibiting cultures of 26 types of bacteria is shown in Table I.

TABLE I.
Inhibition Power of the Crude Extract of the Coptis Root on Bacteria.

Organism	Max. inhibiting dilution
Staph. aureus (2 strains)	1:3200 -1:6400
Staph. citreus (2 strains)	1:6400 -1:12800
Staph. albus	1:12800
Strep. beta hemolyticus	1:3200
Strep. alpha hemolyticus	1:3200
Strep. gamma	1:3200
C. diphtheriae	1:3200 -1:6400
Diphtheroid	1:3200
Klebsiella pneumoniae	1:1600
B. subtilis	1:6400
Micrococcus tetragenus	1:12800
Vibrio comma	1:3200
Shigella dysenteriae (5 strains)	1:400 -1:12800
Shigella sonnei	1:800
Shigella paradysenteriae	1:800
Br. abortus	1:25600-1:51200
Br. melitensis	1:3200
Eberthella typhosa	
H901	0
O901	0
S. paratyphi	0
S. schottmuelleri	0
S. enteritidis	0
E. coli	0
Proteus OX_{19}	0
Pseudomonas pyocyanea	0
Serratia marcesecus	0

0 indicates no inhibition in 1:200.

From Table I, it seems very clear that the crude extract of the coptis root in high dilutions inhibited the growth of all Gram positive organisms tested and also that of certain Gram negative ones. The extract appeared particularly effective against *Br. abortus*, as, even in a dilution of 1:25600, growth of this organism was inhibited. Of some interest is that one strain of *Staphylococcus citreus*, isolated from a patient with carbuncle, and highly resistant toward the action of penicillin (50 U/ml) showed great susceptibility to the crude extract in the dilution of 1:12800. When subcultures were made on blood agar plates, it was shown that the bacteriostatic power of the extract was usually 2-4 times greater than its bactericidal power.

Tests for Toxicity. Adult albino rats of 200 g body weight were injected intraperitoneally with 5% aqueous extract solution and observed at intervals of 10 minutes, 30 minutes, 1 hour and 24 hours after injection. Amounts of 2 and 1.5 ml caused death of the animals in 30 minutes, while those of 1 and 0.5 ml produced no obvious toxic symptoms. The animals remained well in 1 week.

Discussion. The root of coptis has been generally used as a bitter tonic, but, in China, it has been extensively used in the treatment of dysentery since ancient times.[4] Results of *in vitro* tests made in the present study extended those of the previous worker in demonstrating bacteriostatic power against various types of dysentery bacilli and may explain why coptis root has been used empirically by the Chinese. The unexpected finding of the special effectiveness of this extract against our stock strain of *Br. abortus* but not particularly so against *Br. melitensis* requires further study. It may be mentioned that the active principle so far has been found to be completely adsorbed on activated charcoal. Further investigations regarding purification and chemical analysis and *in vivo* tests of this extract are being undertaken.

Summary. The dilute alcohol extract of the coptis root has been demonstrated to have a definite and fairly high antibacterial action

[4] Li, S. C., Catalogue of Native Herbs, A.D. 1596.

against a number of both Gram positive and Gram negative bacteria. Its lethal dose for albino rats has been found to be more than 250 mg per kg body weight.

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Anticoagulant Effect of Dicumarol at Various Prothrombin Levels in Dogs.

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(Introduced by I. S. Ravdin.)

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Since the introduction of dicumarol for clinical use[1] there have been differences of opinion concerning the prothrombin reduction required to produce an adequate anticoagulant effect. Some investigators recommend that the prothrombin level be reduced to 10 to 30% of normal.[2,3,4] Others state that the effective therapeutic prothrombin zone lies between 20 and 60%;[5] 35 and 50%[6] and 50 and 60%.[7]

In 2 reported series of patients in which the prothrombin was reduced to 10 to 30% of normal, hemorrhage occurred in 5%[3] and 6%[4] of the patients. Excessive hypoprothrombinemia (below 10%) occurred in 10 to 20% of patients following doses of dicumarol which usually resulted in 10 to 30% prothrombin levels.[4] It seems probable, therefore, that the maintenance of higher prothrombin levels might be preferable if the anticoagulant effect is adequate at higher levels.

Little experimental work has been done to clarify this problem. In the experiments herein reported the anticoagulant effect of dicumarol at various prothrombin levels in dogs has been studied in order to determine whether there is a definite and consistent correlation between prothrombin levels and anticoagulant activity.

Method. The dogs were anesthetized with intravenous sodium pentobarbital, and the femoral artery was exposed and cannulated with as little trauma as possible. Thrombosis was produced by inserting into the femoral artery a sterile glass cannula 1.0 mm in diameter at its constricted opening. The cannula widened out to a 3.5 mm diameter where it was connected to a mercury manometer by sterile rubber tubing. The entire system was filled with sterile physiological saline solution. Additional saline was introduced through a T side-arm in the tubing to produce a positive pressure approximately equal to the mean arterial blood pressure in order to prevent the passage of blood into the tubing. When thrombosis occurred, the mercury column in the manometer ceased oscillating, and this was taken as the end-point.

The prothrombin level of each dog was determined within two hours of the time it was cannulated by the Quick method, with the plasma diluted 50% with normal physiological saline solution. A normal curve was plotted each day the experiment was performed to eliminate errors due to a variation in the potency of the thromboplastin. Table I expresses the prothrombin times (in seconds) of various percentages of normal plasma (50%

1 Allen, E. V., Barker, N. W., and Waugh, J. M., *J.A.M.A.*, 1942, **120**, 1009.

2 Barker, N. W., *Minnesota Med.*, 1944, **27**, 102.

3 Allen, E. V., *J.A.M.A.*, 1947, **134**, 323.

4 Cosgriff, S. W., Cross, R. J., and Habif, D. V., *Surg. Clin. N. Am.*, April 1948, 324.

5 Levan, J. B., *Ann. Int. Med.*, 1946, **25**, 941.

6 Peters, H. R., Guyther, J. R., and Brambel, C. E., *J.A.M.A.*, 1946, **130**, 398.

7 Cummine, H., *M. J. Australia*, 1947, **34**, 302.