Isolation and identification of the toxic principle from Tetradymia glabrata
by Samuel Kenneth Reeder

A thesis submitted to the Graduate Faculty in partial fulfillment of the requirements for the degree of
DOCTOR OF PHILOSOPHY in Chemistry
Montana State University

Abstract:
Tetradymol, 3,4a(R),5(S)-trimethyl-8a(S)- hydroxy-4,4a 5,6,7,8,8a ,-9-octahydro-naphtho [2,3-b] furan (II), has been isolated from Tetradymia glabrata, a desert plant of the great Salt Lake Basin, which is the cause of extensive range losses of sheep. This compound was shown to be an active principle of the plant by sheep and mouse feeding experiments.

The structure of the compound was established on the basis of chemical and spectral data, and confirmed by an X-ray crystallographic structure of the 2-chloromercury derivative.

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ABSTRACT

Tetradymol, 3,4a(R),5(S)-trimethyl-8a(S)- hydroxy-4,4a5,6,7,8,8a,-9-octahydro-naphtho [2,3-b] furan (II), has been isolated from Tetradymia glabrata, a desert plant of the great Salt Lake Basin, which is the cause of extensive range losses of sheep. This compound was shown to be an active principle of the plant by sheep and mouse feeding experiments.

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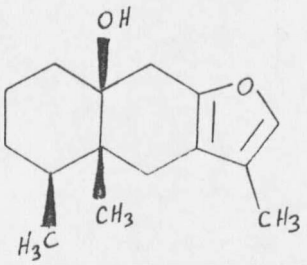

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INTRODUCTION

The living organism is a very complex unit performing a great number of integrated functions, but it could be considered as an integrated chemical plant taking in raw materials and converting them into energy and products that it needs for building and other functions. However, as is the case in most chemical plants, the entering raw materials and the products must be purified of the nonusuable materials and by-products, and these materials must be eliminated.

In mammals there are a number of organs that are responsible for the above type of purification and elimination; the lungs, intestines, kidneys, and liver to name a few. One of these, the liver, is important for purification of the raw materials coming from the digestive tract, removal of some deleterious materials of normal metabolism from the blood, and excretion of these materials or their conjugates by means of the bile duct. These materials, to be excreted, are of many different types and require diverse enzymatic processes for reaction and/or excretion. The liver, thus, plays a very important role in the function of the total system and because of this diversity of function can be injured in many ways.

A brief outline of hepatic function with respect to substances entering the body from the intestine is shown in Figure 1. Food substances and other molecules pass through the intestinal walls into the blood capillaries and are then transported into the portal vein

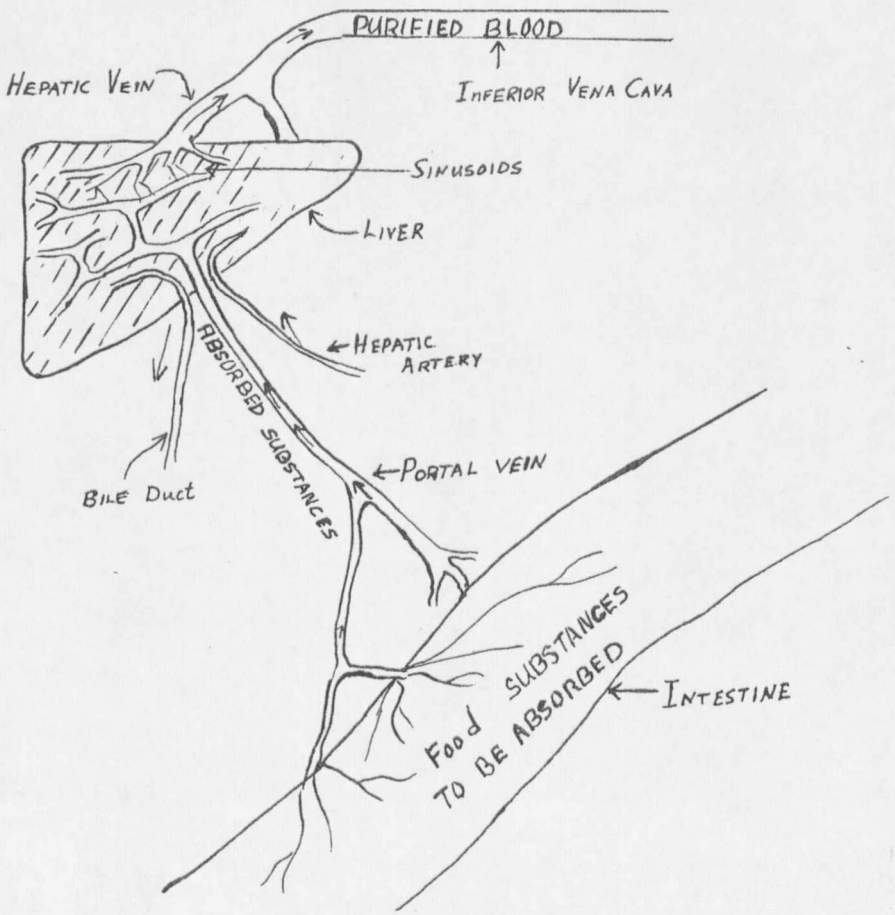

Figure 1. A Diagram of Hepatic Function

which transports them into the liver. Here the blood passes into smaller vessels until it reaches the sinusoids of the lobules. Classically these lobules are the small units of the liver bounded by planes drawn between the lines of the hepatic triad; hepatic artery, portal vein, and bile duct surrounded by Glisson's capsule; centered about the central vein as shown in Figure 2. The purification of incoming blood