$$(1 - H)V = V_w/t \qquad \text{(Eq. 2)}$$

the following is obtained:

$$\int_0^t Cdt = C_w t \qquad \text{(Eq. 3)}$$

By keeping a constant withdrawal of blood and measuring the concentration of drug in the sample and the time of withdrawal, the *AUC* can readily and accurately be determined without the problems of extrapolation.

This method is especially valuable in the time just after administration of an intravenous bolus dose, because no assumptions regarding the distribution and elimination need to be made. At later time points, when it is more desirable to determine the various rate constants, the continuous withdrawal can be terminated and individual blood samples then can be taken.

We have used this method extensively for indocyanine green clearance in rabbits, where the initial half-life after a 0.1-mg/kg iv. bolus dose is ~0.8 min. Approximately 40–60% of the total area can be estimated to be located between 0 and 1 min if an extrapolation is carried out when the first sample is taken at 1 min. However, when a continuous withdrawal is carried out, only 20–30% of the total area is obtained in the first minute. Therefore, as much as a 1.5- to twofold underestimation of the clearance can be made when using single venous plasma concentration time points with extrapolation, rather than a continuous withdrawal technique for indocyanine green clearance in rabbits.

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Schiff Base Formation with Nitrogen of a Sulfonamido Group

Keyphrases □ Benzothiadiazones—Schiff base formation with the nitrogen of a sulfonamido group □ Schiff bases—formation with the nitrogen of a sulfonamido group □ Colored complexes—Schiff base formation with the nitrogen of a sulfonamido group

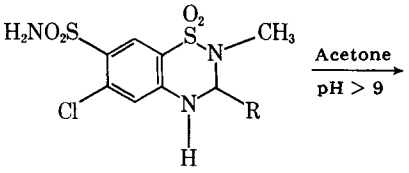
To the Editor:

Recently an unexpected result was reported (1): A violet-colored compound was reported to have formed on TLC plates when benzothiadiazines (I) were sprayed with acidified *p*-dimethylaminobenzaldehyde (II). Hennig *et al.* (1) stated that the type of colored complex formed between I and II was difficult to postulate, since there was no apparent record of Schiff base formation with the nitrogen of a sulfonamido group. We have an explanation that attempts to rationalize the formation of this colored complex.

Our studies with polythiazide (I*a*) have shown that II as well as acidified vanillin (II*a*) form a violet-colored compound. We have identified this compound to be a product of a double aldol condensation between acetone, used as the solvent for spotting I, and II or II*a* to form in each case, respectively, substituted distyryl ketone (V).

Bahner and Schultze (2) reported the formation of divanillylidene acetone (V*a*) in a photometric estimation of acetone. Compound V*a* is yellow in alkaline solutions and develops into a pink-violet color when acidified with hydrochloric acid.

We have noted that at pH 9 polythiazide partially decomposes into 4-amino-2-chloro-5-(methylsulfamyl)-benzenesulfonamide (VI). Compound VI reacts with acetone to form a Schiff base (see Scheme). The ionized form of this Schiff base has an R_f = 0.55 in an ethyl acetate–benzene (8:2) system. When sprayed with acidified vanillin, the Schiff base hydrolyzes and the acetone thus liberated reacts with vanillin to give a violet-colored spot on the chromatograms. A similar reaction takes place with acidified *p*-dimethylaminobenzaldehyde used as a spray reagent.



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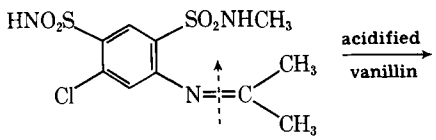
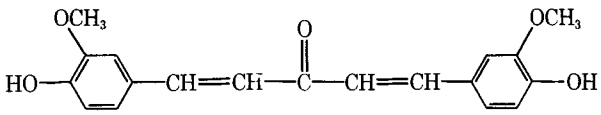


VI schiff base



V*a*

Vanillin is often used as flavoring to mask the unpleasant taste of polythiazide tablets. If the alcohol that is used as a granulating liquid contains acetone as an impurity, the reaction in the Scheme may cause an incompatability problem resulting in colored granules.

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