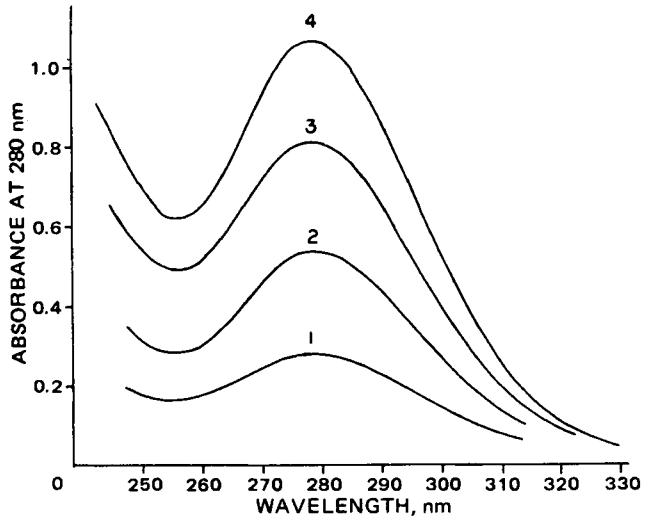

Figure 2—*UV spectra of solutions containing 1 × 10^{-2} M sodium bisulfite and varying amounts of* cis-*platinum. Key: 1, 4 μg/ml; 2, 8 μg/ml; 3, 12 μg/ml; and 4, 16 μg/ml.*

in nonlinear fashion as a function of the bisulfite concentration. Furthermore, in the presence of nitrogen or concentrations of ethanol or methanol as low as 1 × 10^{-3} *M*, no reaction was observed indicating autoxidation.

When 0.5 ml of 1 *M* sodium bisulfite (pH 4.2) was added to different concentrations of *cis*-platinum (0.1–0.5 ml of 1 mg of *cis*-platinum/ml) in water and the reaction mixture was left for 5 min at room temperature and diluted with pH 4.2 acetate buffer to 25 ml, the maximum absorbance at 280 nm varied linearly with the *cis*-platinum concentration (Fig. 2).

The absorbance at 280 nm remained constant for several hours. Although the exact mechanism of this interesting reaction is not known at this time, such a chemical reaction possibly may occur *in vivo* between the antitumor agent and the enzymes containing a sulfhydryl group found in the body.

Furthermore, in view of the enhancement of the UV absorbance of *cis*-platinum in the presence of bisulfite, this reaction can be used for the analysis of the drug in dosage forms. This observation also is important from the pharmaceutical standpoint when the drug is added to intravenous fluids containing antioxidants such as sodium bisulfite. It may be possible that the antioxidant will inactivate the drug in the intravenous fluids prior to administration.

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Percutaneous Absorption of Nitroglycerin

Keyphrases □ Nitroglycerin—percutaneous absorption, rhesus monkeys □ Absorption, percutaneous—nitroglycerin, rhesus monkeys □ Vasodilators—nitroglycerin, percutaneous absorption, rhesus monkeys

To the Editor:

We wish to report the percutaneous absorption of nitroglycerin in the rhesus monkey, an animal model that has been shown to be similar to humans (1, 2).

Sublingual nitroglycerin therapy has been the principal treatment for the symptomatic relief of angina pectoris. Sublingual nitrates are very effective, but their symptomatic improvements are not long lasting. Recently, nitroglycerin administered topically as an ointment was shown to be clinically effective for angina (3), and the slower absorption rate after topical administration results in a longer duration of action than after sublingual administration. Oral administration of nitroglycerin is not effective.

Our objective was to study some parameters of the percutaneous absorption of nitroglycerin. We wanted first to determine if there is an optimal site for absorption because the anatomical site of application affects skin absorption (4, 5). We then wanted to ascertain if the size of the application area affects the absorption of nitroglycerin.

The study was done *in vivo* with the rhesus monkey (*Macaca mulata*). Nitroglycerin (40 mg, 5 μCi) labeled with carbon 14 was applied to a 2-cm^2 area of skin. The areas tested were the chest, arm (upper inside), inner thigh, and postauricular region. After the application, each area was occluded with aluminum foil and adhesive tape for 24 hr. Then the occlusion was removed, and the site was washed with soap and water.

In addition, absorption of an identical dose was determined on the chest using a surface area of 50 cm^2. For this larger surface area, it was necessary to dissolve the dose in 250 μl of absolute ethanol. This solution was applied, and the ethanol was gently evaporated. Alcohol does not significantly alter nitroglycerin absorption (6). Percutaneous absorption was determined by the urinary excretion of carbon 14.

Absorption was quantified on the basis of the percent of radioactivity excreted in urine for 5 days following application of a known amount of the labeled compound to the skin. Daily urinary excretion values were corrected for excretion of radioactivity by other routes and retention of radioactivity in the body by administration of an intravenous dose of [^{14}C]nitroglycerin (1). Urinary radioactivity represents only the apparent nitroglycerin absorption. The potential for skin metabolism of nitroglycerin during absorption is unknown.

After intravenous administration of [^{14}C]nitroglycerin, 59.0 ± 1.9 (*SEM*) % of the dose was excreted in the urine in 5 days. Percent absorptions were 13.4 ± 1.2 (chest), 12.9 ± 1.2 (arm), 8.9 ± 1.4 (postauricular), and 14.8 ± 2.2 (thigh). None of the absorption values for doses applied to the 2-cm^2 areas was statistically different from each other. The majority of the unabsorbed dose in each case was recovered in the wash. Absorption of an identical dose

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on the chest from a surface area of 50 cm^2 was significantly ($p < 0.002$) greater (36.4 ± 4.3%) than the absorption from the smaller surface area. Therefore, differences in these anatomical sites did not affect absorption, but increasing the size of the skin surface area did increase absorption.

The anatomical site of application has been shown to affect the percutaneous absorption of compounds in humans (4, 5) and the rhesus monkey (7). Site dependence for absorption of nitroglycerin has been reported in the rat (8) and humans (9). In the human study, the topical dose and the surface area were not controlled, but both of these parameters affect absorption (2).

Two points should be stressed. First, the topical dose and the surface area must be controlled in percutaneous absorption studies. Second, future studies may show that nitroglycerin absorption can vary with some anatomical sites. However, there also will be anatomical sites where absorption is similar. Therefore, a patient may have the convenience of choosing a preferred site.

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BOOKS

REVIEWS

GLC and HPLC Determination of Therapeutic Agents, Parts I–III. (Chromatographic Science Series, Vol. 9).

Part I edited by K. TSUJI and W. MOROZOWICH.

Parts II and III edited by K. TSUJI.

Dekker, 270 Madison Ave., New York, NY 10016.

Part I: 1978, 415 pp., 18 × 26 cm, Price $37.50.

Part II: 1978, 432 pp., 18 × 26 cm, Price $45.00.

Part III: 1979, 528 pp., 18 × 26 cm, Price $45.00.

Part I has chapters entitled: Theory and Instrumentation, Column Selection in GLC, Column Selection in HPLC, Derivatization Techniques in Gas–Liquid Chromatography, Derivatization Techniques in HPLC, The Mass Spectrometer as a Detector for Gas–Liquid Chromatography, Isolation of Samples Prior to Chromatography, Preparative HPLC: Small Scale and Trace Collection, Preparative HPLC: Milligram Quantities, Quality Control in GLC, Automation and Quality Control in HPLC, Computer Interfacing, and Data Processing. Much new material as well as an exhaustive critical review of the literature is included. The writing has an immediacy and authority which are most welcome, indicating that the authors are directly involved with the techniques they describe. The volume is recommended to all in the field who wish to update their knowledge of the theory and practice of GLC and HPLC. It is particularly recommended to graduate students and would make an excellent course text except for one problem: an index is available only in Part III. Use of the index is made more annoying since the three parts are successively paginated so that the index does not immediately indicate the volume to open.

Part II is devoted to therapeutic drug monitoring with GLC and HPLC. It contains chapters 14–24, which give scientific methods and detailed directions for individual drugs. In addition to the literature review, there are author-preferred-and-tested methods for each drug. The drug classes covered are: narcotic analgesics, narcotic antagonists and related drugs, central nervous system (CNS) depressants, cocaine and phenylethylamines, hallucinogens, cannabis preparations, barbiturates, anticonvulsants, salicylates, aniline derivatives, pyrazolones, synthetic opiate-like drugs of low potency and low addictive potential, analgesic combinations, nonbarbiturate hypnotics, glutethimide, methaqualone, anorexigenics, antipsychotics, antianxiety agents, antidepressives, stimulants, antihypertensives, pulmonary and vasoactive drugs, antimicrobials, antimycotics, antiparasitics, adrenocorticosteroids, androgens, estrogens, and antifertility steroids. In addition, there are chapters on preservatives and on the determination of residues in gaseous sterilants.

The editor has been extremely careless in Part II, allowing the same material about the same drug to appear in two different chapters. For example, Fig. 9 of Chapter 14, showing GLC analysis of opium alkaloids, is reproduced as Fig. 15 of Chapter 16. The duplicated information involves the narcotic analgesics, barbiturates, amphetamine, papaverine, and, perhaps, others.

Part III continues with the drugs used in metabolic diseases, those that affect endocrine functions and nutritional agents. Drug classes included are: nonsteroidal anti-inflammatories, prostaglandins, cardiac glycosides, antiarrhythmics, vasodilators, oral anticoagulants (there are no methods for heparin in this collection), antidiabetics, diuretics, lipid- and cholesterol-lowering agents, thyroid agents, X-ray contrast agents, nucleosides and nucleotides, alkaloids, antihistamines and antitussives, water-soluble vitamins, fat-soluble vitamins, amino acids and peptides, sugar and sugar alcohols, and saccharin. The last chapter deals with serum lipid and fatty acid analysis.

The methods reported in Parts II and III include sample preparation (including separation from clinical samples or drug formulations and derivatization) as well as the determinations. Most chapters contain a summary table of the drugs included in it, choosing between GLC and HPLC as the method of choice and giving the chromatographic conditions.

It is an amusing coincidence that while this review was being prepared, the August issue of "Chromatography Newsletter" was received, which was devoted entirely (15 pages) to drug analysis, thus showing again that reviews, no matter how well done, can only supplement and not substitute for current periodicals.

These three volumes are an indispensible reference to all scientists who use or intend to use GLC and HPLC, particularly drug analysts, forensic scientists, clinical chemists, and biochemists. Good use of the collection will be made by "anyone concerned with the potency, purity, stability,