Ascorbic Acid Absorption in Humans: A Comparison among Several Dosage Forms

SUSANNA YUNG ‡, MICHAEL MAYERSOHN *x, and J. BARRY ROBINSON ‡

Received May 11, 1981, from the * *Department of Pharmaceutical Sciences, College of Pharmacy, University of Arizona, Tucson, AZ 85721* and the ‡ *Faculty of Pharmacy, University of Toronto, Toronto, Ontario, Canada.* Accepted for publication July 20, 1981.

Abstract □ There have been few studies conducted to determine the efficiency of ascorbic acid absorption in humans. Differences in the extent of its absorption among individuals may contribute to the outcome of clinical trials. Ascorbic acid absorption in four subjects was investigated from several oral dosage forms containing 1 g of the vitamin (solution, tablet, chewable tablet, and timed-release capsule). Approximately 85% of an intravenous dose was recovered in the urine as ascorbic acid and its major metabolites. In contrast, only ~30% of the dose was recovered from the solution and tablet forms. A considerably smaller fraction of the dose (~14%) was recovered from the timed-release capsule. There was considerable intersubject variation in ascorbic acid absorption and there appeared to be good and poor absorbers of the vitamin. Consideration should be given to the influence of the extent of ascorbic acid absorption on the results of clinical trials.

Keyphrases □ Ascorbic acid—comparison of absorption of several dosage forms, humans □ Absorption—ascorbic acid, comparison of several dosage forms, humans □ Vitamin C—comparison of absorption of several dosage forms, humans

Since the claim (1–3) that the daily consumption of large quantities of ascorbic acid may have beneficial effects for such conditions as the common cold, numerous investigations have been conducted to evaluate the efficacy of large doses of this vitamin for reducing the frequency and duration of cold symptoms (4–8). The results of these studies remain controversial (9, 10) although there is at least some tentative support for the clinical claims. Several studies have been criticized for lack of adequate control and for poor experimental design, factors which may have substantially influenced their results and conclusions. Perhaps equally as important is an understanding and the proper control of variables that may affect the absorption or bioavailability of the vitamin from the oral form. At present little is known about the absorption and disposition of ascorbic acid administered exogenously. Since ascorbic acid appears to be absorbed in humans by a specialized process (11, 12), the rate and extent of its absorption may be influenced by the relative efficiency of different oral dosage forms, size of the dose, and physiological conditions along the GI tract. The present study was designed to examine ascorbic absorption from various commercially available oral dosage forms.

EXPERIMENTAL

Protocol—Four healthy adult subjects participated in the study (three males and one female, 25–32 years of age) after giving informed written consent. Each subject ingested 1 g of ascorbic acid/day for a period of not less than 2 weeks prior to the experiments, in order to saturate body stores of the vitamin. Saturation of body stores was determined in the following manner. After the 2-week dosing period, 1 g of ascorbic acid (powder dissolved in water) was ingested on an empty stomach. Total urine was collected for the subsequent 24 hr and assayed for total vitamin. This procedure was repeated 3–7 days later. Between these two test doses the subjects ingested 1 g of ascorbic acid/day. The body stores were accepted as being saturated if the total amount of vitamin excreted during 24 hr from each test dose was within ±10% of each other.

Two days prior to and during an experimental day the subjects avoided the ingestion of ascorbic acid either in the form of vitamin preparations or foods known to be high in ascorbic acid content. One day prior to the experiment, blank urine samples were obtained by collecting total urine for several hours during two collection periods (one in the morning and one in the afternoon). The bladder was voided at the beginning of the collection period and the exact time of the collection interval and urine volume was noted.

On the experimental day the subjects ingested the assigned dosage form of the vitamin on an empty stomach after an overnight fast. Food was withheld for the next 3–4 hr. The dosage forms were ingested with 200 ml of water. The chewable tablets were thoroughly chewed prior to swallowing. The dosage forms ingested were:

A. 1 g of ascorbic acid powder dissolved in water[1]
B. 1 g of ascorbic acid tablets[2] (two 500-mg tablets)
C. 1 g of ascorbic acid chewable tablets[3] (two 500-mg tablets)
D. 1 g of ascorbic acid timed-release capsules[4] (two 500-mg capsules)

Each subject was randomly assigned to a specific schedule for ingestion of the different dosage forms according to a 4 × 4 Latin square design. In addition to the above dosage forms, 1 g of ascorbic acid was given intravenously 1 week after the completion of these experiments. The injectable solution[5] (4 ml) was injected into an arm vein over 3–4 min (500 mg/2-ml vial).

The bladder was voided immediately after drug administration. Urine was then collected during frequent and known time intervals during the subsequent 24 hr. The total volume of each collection was recorded and a 15-ml aliquot was taken and transferred to a vial which contained sufficient metaphosphoric acid such that a 4% solution of the acid was obtained with 15 ml of urine. The vial was shaken to dissolve the acid and stored in a refrigerator and assayed within 4 days. After the 24-hr collection period, the subjects resumed daily ingestion of 1 g of ascorbic acid until 2 days prior to the next experiment. A period of 1 week elapsed between successive experiments.

Analytical—All dosage forms were assayed to determine ascorbic acid

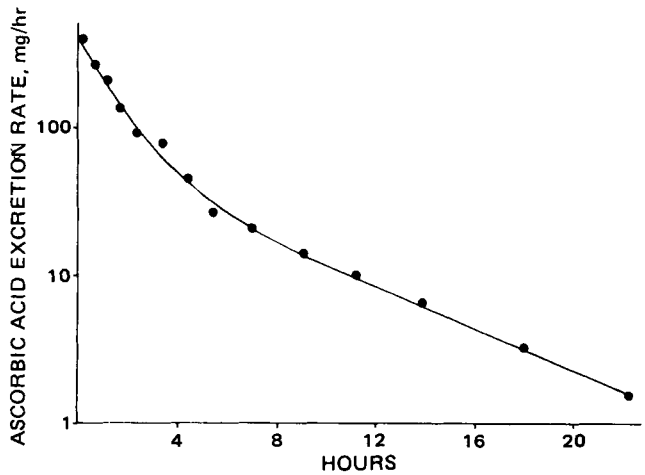

Figure 1—*Urinary excretion rate of ascorbic acid as a function of time in one subject after the intravenous injection of 1 g of ascorbic acid. The solid line represents the best fit of the data.*

[1] Lot 53808, BDH Chemicals, Ltd., Toronto, Ontario, Canada.
[2] Lot 509731, Novopharm Ltd., Scarborough, Ontario, Canada.
[3] Lot 505434, Novopharm Ltd., Scarborough, Ontario, Canada.
[4] Lot NDC 0817-0015-25, Ascorbicap, ICN Pharmaceuticals, Cincinnati, Ohio.
[5] Lot 7509-1, Sterilab Corp., Ltd., Downsview, Ontario, Canada.

0022-3549/82/0300-0282$01.00/0

Table I—Bioavailability of Ascorbic Acid from Various Dosage Forms

Subject	Percentage of Dose Recovered: Dosage Form: Solution	Tablet	Chewable Tablet	Timed-Release Capsule	Intravenous
1	16.1	10.7	12.2	6.2	81.3
2	34.9	44.2	26.1	17.4	84.6
3	23.4	19.0	24.6	10.9	85.7
4	54.2	45.3	58.8	22.6	87.3
Mean	32.1	29.8	30.4	14.2	84.7
±*SD*	16.6	17.6	19.9	7.2	2.5

content according to USP methods (13). Urine was assayed by the 2,4-dinitrophenylhydrazine method outlined by Pelletier (14) to determine concentrations of ascorbic acid and its two major metabolites, dehydroascorbic acid and diketogulonic acid. This assay method is based upon the formation of a colored osazone from dehydroascorbic and diketogulonic acids and it offers a means of differentiating the three compounds. The final solutions were measured colorimetrically at 520 nm. Concentrations of the compounds were determined from previously prepared standard curves and amounts excreted during a collection interval were calculated from the product of concentration and urine volume. The urinary excretion data were corrected for blank values determined from the urine samples collected on the day prior to each experiment.

Data Analysis—Urinary excretion data were used to calculate ascorbic acid excretion rate as a function of time. Initial estimates of the absorption rate constant (K_a) and the elimination rate constant (K) were obtained from semilogarithmic graphs of excretion rate *versus* time by the method of residuals. Using these initial estimates, the data obtained after the oral administration of ascorbic acid were fit by nonlinear regression analysis employing the equation appropriate for a one-compartment model and assuming first-order absorption and elimination. Since the urinary excretion data suggested the existence of a lag time (T_{lag}) between the time of dosing and the time when ascorbic acid excretion began, the equation incorporated T_{lag} as a parameter to be estimated. The computer-generated values for the above parameters were used to calculate the maximum excretion rate (ER_{max}) and the time of occurrence of this maximum (T_{max}). The excretion rate *versus* time data obtained after intravenous administration of the vitamin were fit to the equation appropriate for a two-compartment model. Initial estimates of the coefficients and exponents of the equation were obtained graphically using the method of residuals. These data were then fit by nonlinear regression analysis as already mentioned.

The bioavailability or extent of ascorbic acid absorption from each of the forms administered was determined from the total amount of the vitamin excreted into the urine during 24 hr (*i.e.*, the sum of ascorbic, dehydroascorbic, and diketogulonic acids). This value was then corrected for the actual dose ingested based on the assay of the dosage forms. Similarly, since ER_{max} depends on the actual dose ingested, this value was corrected for the actual assayed content of the vitamin. The extent of absorption was expressed either as a percentage of the dose recovered or as a percentage of the intravenous dose recovered.

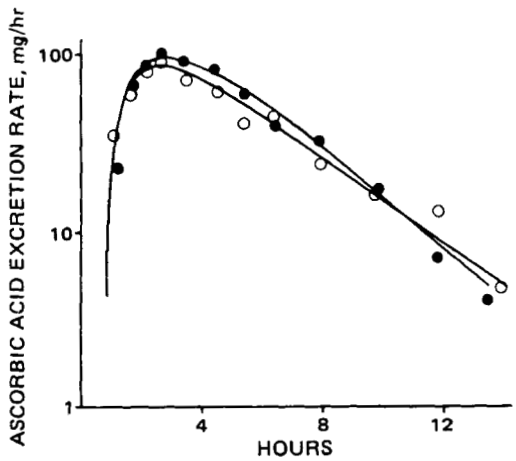

Figure 2—*Urinary excretion rate of ascorbic acid as a function of time in one subject after the ingestion of 1 g of ascorbic acid as a solution (●) or as a tablet (○). The solid lines represent the best fit of the data.*

Table II—Maximum Ascorbic Acid Excretion Rate (ER_{max}) from Various Dosage Forms

Subject	Maximum Excretion Rate, mg/hr: Dosage Form: Solution	Tablet	Chewable Tablet	Timed-Release Capsule
1	35.8	20.2	25.5	6.4
2	54.5	49.7	45.5	24.0
3	46.9	43.0	43.5	16.6
4	96.2	77.5	98.1	30.1
Mean	58.4	47.6	53.1	19.3
±*SD*	26.4	23.6	31.3	10.2

The percentage availability of ascorbic acid, ER_{max} and T_{max}, were statistically analyzed to determine any differences among the dosage forms examined. These data were analyzed according to a 4 × 4 Latin square design (15). Variance ratios were calculated for comparisons among dosage forms, subjects, and sequence of administration. Scheffe's test (16) was also employed to contrast these parameters.

RESULTS AND DISCUSSION

Standard curves for ascorbic acid in urine were linear and reproducible over the concentration range of 2–40 μg/ml. By repetitively assaying urine containing a known concentration of ascorbic acid (with 4% metaphosphoric acid and stored in a refrigerator) it was determined that the vitamin was stable for at least 4 days.

The mean assayed contents of ascorbic acid determined from 20 samples of the oral dosage forms were (expressed as percent of label claim): powder, 99.9%; tablet, 107.8%; chewable tablet, 101.2%; and timed-released capsule, 104.3%. The injectable solution contained 108.7% of the label claim based on the assay of three vials. The urinary excretion data were corrected for these values of actual ascorbic acid content.

The results of the intravenous experiments were previously reported elsewhere (17). Figure 1 is a representative graph of ascorbic acid excretion rate as a function of time after intravenous administration to one subject. The data appear to be consistent with a two-compartment model. The average elimination $t_{1/2}$ associated with the log-linear terminal exponential phase (β-phase) was 3.5 hr (range, 2.7–4.3 hr). The percentage of the intravenous dose recovered in the urine averaged 84.7% (range, 81.3–87.3%) as shown in Table I. Figures 2–4 are representative graphs of ascorbic acid excretion rate as a function of time after the oral ingestion of the various dosage forms studied. For comparison, the data obtained from the oral solution are included in each graph. The excretion rate–time profiles are similar for the oral solution, tablets, and chewable tablets. A comparable pattern is not seen, however, for the timed-release preparation. In the latter case, the rate of absorption and ER_{max} are considerably smaller compared with the other oral dosage forms.

The bioavailability of the vitamin from these dosage forms is summarized in Table I. The solution, tablet, and chewable tablet are absorbed to approximately the same extent (~30% of the dose) although there is considerable intersubject variation in the percentage of the dose recov-

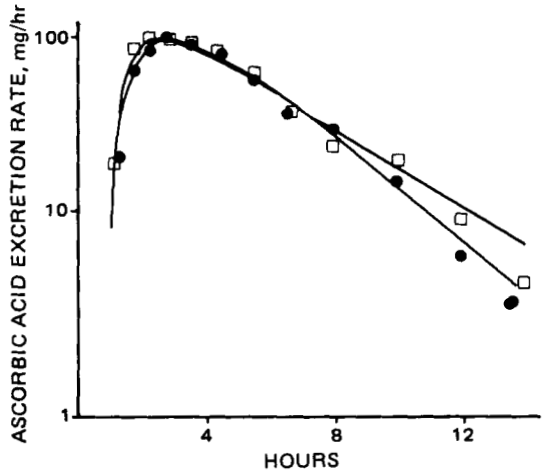

Figure 3—*Urinary excretion rate of ascorbic acid as a function of time in one subject after the ingestion of 1 g of ascorbic acid as a solution (●) or as a chewable tablet (□). The solid lines represent the best fit of the data.*

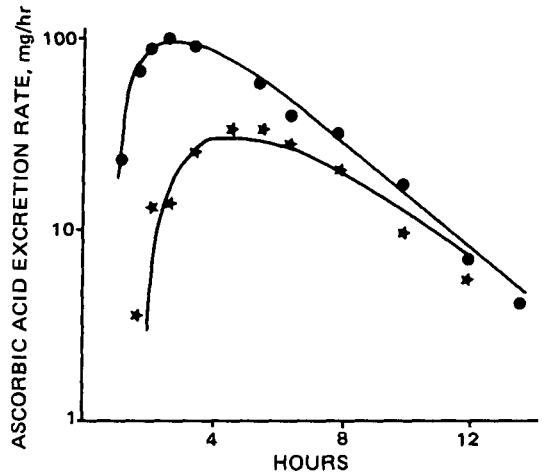

Figure 4—*Urinary excretion rate of ascorbic acid as a function of time in one subject after the ingestion of 1 g of ascorbic acid as a solution (●) or as a timed-release capsule (★). The solid lines represent the best fit of the data.*

ered. Absorption from the timed-release capsule is considerably less than from the other dosage forms (~14% of the dose). Based on analysis of variance there is a statistically significant difference among subjects with respect to the percentage of the oral dose recovered ($p < 0.01$) but there was not a statistical difference with respect to sequence of administration ($p > 0.25$). Percentage recoveries among the oral dosage forms were not statistically different ($0.05 < p < 0.10$), probably as a result of the large variation in these values among the subjects. Since the urinary recovery data suggested that the timed-release capsule was considerably different from the other oral dosage forms, Scheffe's test (16) was used to compare the means obtained from the timed-release capsule *versus* the other forms. As with the analysis of variance, the difference was close to but did not reach statistical significance.

A comparison of maximum ascorbic acid excretion rate (ER_{max}) among the different dosage forms is presented in Table II. These values have been normalized for the assayed content of ascorbic acid in each form. Analysis of variance indicated significant differences among the products ($p < 0.01$) and among subjects ($p < 0.01$), while there was no significant difference with respect to sequence of administration ($p > 0.25$). The timed-release capsule had a substantially lower ER_{max} value compared to the other oral dosage forms.

Table III summarizes the times needed to achieve maximum excretion rates (T_{max}). Consistent with a slower absorption rate noted for the timed-release capsule, T_{max} for this form was significantly prolonged ($p < 0.01$) compared with the other oral dosage forms. There were no statistically significant differences among subjects or as a result of administration sequence.

Prior to the evaluation of ascorbic acid absorption from the various dosage forms examined, all subjects were shown to be saturated with the vitamin. This approach is necessary in evaluating the absorption of the vitamin from urinary excretion data, since the retention of the vitamin in the body is influenced by the nutritional status of the individual (18–20).

The urinary recovery values of the vitamin were very similar among the subjects after intravenous administration. An average of 85% of the dose was ultimately recovered in the urine. The remainder of the dose may be accounted for by other minor metabolites of the vitamin not detected by the assay method (*e.g.*, oxalic acid and ascorbate-2-sulfate) (21, 22) or a portion of the dose may remain in the ascorbate pool.

In contrast to the intravenous data, there was considerable variation in the urinary recovery of the vitamin after oral ingestion (Table I). With any given oral dosage form there is large variation in the excretion of the vitamin among the subjects. There appeared to be a trend in this variation in that subject 1 consistently excreted less vitamin and subject 4 consistently excreted more vitamin than the other subjects. While the conclusions presented here are necessarily limited by the number of subjects that participated, the data suggest that there may be "poor" and "good" absorbers of ascorbic acid. This trend is best supported by the oral solution data where there are no dosage form effects (*e.g.*, disintegration and dissolution processes) to mask the inherent ability to absorb the vitamin. When dissolved in water the vitamin is presented to absorption sites of the GI tract in a form optimal for absorption.

Table III—Time of Maximum Ascorbic Acid Excretion Rate (T_{max}) from Various Dosage forms

	Time of Maximum Excretion Rate, hr			
	Dosage Form			
Subject	Solution	Tablet	Chewable Tablet	Timed-Release Capsule
1	3.1	2.3	2.6	4.9
2	2.3	3.8	2.4	3.8
3	2.1	2.5	3.1	3.5
4	3.0	2.7	2.5	4.5
Mean	2.6	2.9	2.7	4.2
±*SD*	0.5	0.6	0.3	0.6

It was suggested that ascorbic acid is absorbed in humans by a specialized transport mechanism (11, 12). Differences among individuals in the values of the parameters associated with this transport process may partially account for the variation noted in the extent of absorption. Furthermore, differences in physiological variables along the gut (*e.g.* gastric emptying rate) may contribute to this intersubject variation. The absolute absorption of the vitamin from oral solution may be calculated by the ratio of urinary recoveries from the solution to the intravenous dose. Approximately 40% of the dose ingested as a solution is absorbed (range, 20–62%). Compounds transported by specialized processes are generally absorbed only at certain sites along the GI tract. This has been shown, for example, for riboflavin where absorption proceeds from the upper regions of the small intestine (23). The same observation is likely to apply to ascorbic acid. As a result, factors altering gastric emptying and intestinal transit rates (*e.g.*, food and drugs) may influence the efficiency of absorption from the oral dosage form. This effect was adequately illustrated for riboflavin (23, 24) and appears to be the case for ascorbic acid as well (25).

The urinary recovery data indicated that the vitamin was absorbed to approximately the same extent from the solution, tablet, and chewable tablet. The timed-release capsule, however, was absorbed to a much smaller extent compared with the other oral forms. The absolute percentage of the dose absorbed from this capsule was ~17%, which is less than one-half the amount absorbed from the solution (~40%). Several reasons may be suggested to account for the poor absorption of the vitamin from the timed-release capsule. The vitamin may be incompletely released from the formulation resulting in reduced absorption compared with a solution. An additional explanation may be that, to be well absorbed, the vitamin must be released from the formulation and be in solution before the vitamin passes its sites of maximal absorption. Since timed-release formulations are designed to release a compound slowly over an extended period of time, a substantial portion of the dose of the vitamin may not have been released before passing this site. This would be particularly true if, as it appears (26), the major site for absorption is in the upper region of the small intestine.

Further insight into the absorption of ascorbic acid may be obtained by reference to Tables II and III. While the ER_{max} values are similar among the solution, tablet, and chewable tablet forms, the timed-release capsule provides considerably smaller values (Table II). These smaller values for the capsule indicate slower and less complete absorption of the vitamin. The slower and prolonged rate of absorption in contrast to the solution is illustrated in Fig. 4. Also consistent with this slower rate of absorption is the fact that it takes longer for the timed-release capsule to achieve the maximum excretion rate compared with the other oral forms (Table III and Fig. 4). The average value of T_{max} for the timed-release product (4.2 hr) is similar to the value of 4.9 hr reported (27) for a different timed-release formulation of ascorbic acid. Consistent with this discussion are the differences in the apparent first-order absorption rate constant among the dosage forms. The apparent absorption rate constants for the solution (1.4 hr^{-1}), tablet (1.4 hr^{-1}), and chewable tablet (1.3 hr^{-1}) forms are about three times larger than that for the timed-release product (0.4 hr^{-1}).

The results of this study are consistent with the findings of Richards *et al.* (28) who reported greater ascorbic acid plasma concentrations after oral administration of a nonsustained-release product compared with those achieved with a sustained-release product. Similar results were reported by Allen (29) who examined the same timed-release product used in this study. In that study, however, there was no crossover among subjects and the body store of the vitamin was relatively low. The latter point is supported by the small recovery of the vitamin in urine (~3% of the dose for the regular capsule and 1% for the timed-release product). The present findings disagree, however, with those of Zetler *et al.* (27) who measured ascorbic acid blood concentrations and urinary excretion

after oral ingestion of a capsule and a sustained-release product. Their results indicated that the extent of absorption from the sustained-release product was almost twice that from a regular capsule. In addition, ~98% of the sustained-release dose was absorbed compared to an intravenous dose. The latter value is unusually high and we are not aware of any study where an oral dose of ascorbic acid is virtually completely absorbed. Another discrepancy is that the ascorbic acid half-life was determined (27) to be ~11 hr prior to saturation and 29 hr after saturation. These values are considerably greater than those reported for the half-life of the vitamin after exogenous administration (11, 17, 26, 30). The reason for the substantial differences in half-life and availability from the timed-release products reported here and by Zetler *et al.* (27) is not known.

The results of this study indicate that ascorbic acid absorption is incomplete after oral ingestion and that there is considerable intersubject variation in the extent of absorption. In addition, absorption of the vitamin is considerably less efficient from the timed-release capsule examined here compared with the other oral forms. These findings have several implications. From a practical point of view, efficient oral therapy with the vitamin can be achieved by dissolving powdered ascorbic acid in water. In addition, for the specific manufacturers' products examined in this study, tablets and chewable tablets appear comparable to a solution of the vitamin. This conclusion may not apply to tablets made by all manufacturers but that can only be determined from the evaluation of other products in a manner used in the present study. The timed-release capsule examined here appears to be a more expensive and less reliable means of providing oral vitamin therapy compared with other more conventional dosage forms. This conclusion may apply to similar dosage forms which attempt to delay or sustain the release of the vitamin; therefore, bioavailability studies for such forms are essential.

A question that remains to be answered is to what extent does variation in ascorbic acid absorption influence the results of large-scale trials designed to examine the clinical effects of the vitamin? To the authors' knowledge no consideration has been given to absorption as a parameter potentially influencing the findings of such studies. Investigators pursuing such trials should give some consideration to the possible influence of variation in ascorbic acid absorption on clinical outcome.

REFERENCES

(1) L. Pauling, "Vitamin C and the Common Cold," Freeman, San Francisco, Calif., 1970.

(2) L. Pauling, *Proc. Natl. Acad. Sci., USA*, 68 2678 (1971).

(3) L. Pauling, *Am J. Clin. Nutr.*, **24**, 1294 (1971).

(4) T. W. Anderson, D. B. W. Reid, and G. H. Beaton, *Can. Med. Assoc. J.*, **107**, 503 (1972).

(5) T. W. Anderson, G. Suranyi, and G. H. Beaton, *ibid.*, **111**, 31 (1974).

(6) T. W. Anderson, G. H. Beaton, P. N. Corey, and L. Spero, *ibid.*, **112**, 823 (1975).

(7) T. R. Karlowski, T. C. Chalmers, L. D. Frenkel, A. Z. Kapikian, T. L. Lewis, and J. M. Lynch, *J. Am. Med. Assoc.*, **231**, 1038 (1975).

(8) T. L. Lewis, T. R. Karlowski, A. Z. Kapikian, J. M. Lynch, G. W. Schaffer, and D. A. George, *Ann. N.Y. Acad. Sci.*, **258**, 505 (1975).

(9) T. C. Chalmers, *Am. J. Med.*, **58**, 532 (1975).

(10) M. H. M. Dykes and P. Meier, *J. Am. Med. Assoc.* **231**, 1073 (1975).

(11) W. Kubler and J. Gehler, *Int. Z. Vitaminforsch.*, **40**, 442 (1970).

(12) M. Mayersohn, *Eur. J. Pharmacol.* **19**, 140 (1972).

(13) "The United States Pharmacopeia," 19th rev. Mack Publishing Co., Easton, Pa. 1974, pp. 36–38.

(14) O. Pelletier, *J. Lab. Clin. Med.*, **72**, 674 (1968).

(15) G. W. Snedecor and W. G. Cochran, "Statistical Methods," Iowa State University Press, Ames, Iowa, 1973, pp 312–317.

(16) *Ibid.*, 1973, pp 268–271.

(17) S. Yung, M. Mayersohn, and J. B. Robinson, *J. Pharm. Sci.*, **67**, 1491 (1978).

(18) J. M. Faulkner and F. H. L. Taylor, *J. Clin Invest.*, **17**, 69 (1938).

(19) L. J. Harris and S. N. Ray, *Lancet*, **1**, 71 (1935).

(20) S. W. Johnston and S. S. Zilva, *Biochem. J.*, **28**, 1393 (1934).

(21) E. M. Baker, D. C. Hammer, S. C. March, B. M. Tolbert, and J. E. Canhan, *Science*, **173**, 826 (1971).

(22) B. M. Tolbert, M. Downing, R. W. Carlson, M. K. Knight, and E. M. Baker, *Ann. N.Y. Acad. Sci.*, **258**, 48 (1975).

(23) G. Levy and W. J. Jusko, *J. Pharm. Sci.*, **55**, 285 (1966).

(24) W. J. Jusko and G. Levy, *ibid.*, **56**, 58 (1967).

(25) S. Yung, M. Mayersohn, and J. B. Robinson, *Life Sci.*, **28**, 2505 (1981).

(26) J. S. Stewart and C. C. Booth, *Clin. Sci.*, **27**, 15 (1964).

(27) G. Zetler, G. Seidel, C. P. Siegers, and H. Ivens, *Eur. J. Clin. Pharmacol.*, **10**, 273 (1976).

(28) T. W. Richards, E. Cheraskin, and W. M. Ringsdorf, *Int. J. Vitam. Res.*, **39**, 407 (1969).

(29) E. S. Allen, *Curr. Ther. Res.*, **11**, 745 (1969).

(30) J. Gehler and W. Kubler, *Int. Z. Vitaminforsch.*, **40**, 454 (1970).

Mass Spectral Fragmentation of 24,24-Diphenyl-23-ene Derivatives of Cholic Acid

JERRY RAY DIAS

Received December 8, 1980, from the *Department of Chemistry, University of Missouri–Kansas City, Kansas City, MO 64110.* Accepted for publication June 30, 1981.

Abstract □ After electron impact in the mass spectrometer, 24,24-diphenyl-23-ene derivatives of cholic acid ejected the 17-sidechain as an ionized 1,1-diphenyl-butadiene derivative, and the 12α-acetoxy group activated this loss. This contrasts markedly with the mass spectrometric fragmentation of typical sterols having unsaturated 17-sidechains that are also devoid of functionality on the C-ring.

Keyphrases □ Mass spectra—fragmentation of 24, 24-diphenyl-23-ene derivatives of cholic acid □ Cholic acid—24, 24-diphenyl-23-ene derivatives, fragmentation by mass spectra □ Derivatives—24, 24-diphenyl-23-ene derivatives of cholic acid, mass spectral fragmentation

During the course of other investigations (1), a number of 24,24-diphenyl-23-ene derivatives of cholic acid having structural similarities to known biologically active compounds were prepared. Since the Barbier–Wieland 17-sidechain degradation is used extensively in steroid-terpenoid synthesis (2, 3) and electron impact induced loss of the 17-sidechain is of both fundamental and diagnostic importance (4–6), the observations concerning mass spectral cleavage processes of the Barbier–Wieland modified 17-sidechain of steroids and terpenoids are summarized.

RESULTS AND DISCUSSION

The preparation of the compounds in this study was unexceptional. However, isolation of pure diene (IV*a*–IV*d*) was difficult because unreacted monoene was invariably present. Also, it is likely that *E* and *Z*

0022-3549/82/0300-0285$01.00/0