Oral Doxycycline in the Management of Acne Vulgaris: Current Perspectives on Clinical Use and Recent Findings with a New Double-scored Small Tablet Formulation

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ABSTRACT

Oral antibiotics have been used for the treatment of acne vulgaris for six decades. Among dermatologists, tetracyclines represent at least three-fourths of the oral antibiotics prescribed in clinical practice. Unlike other specialties, antibiotic use in dermatology is predominantly for the treatment of noninfectious disorders, such as acne vulgaris and rosacea, which usually involves prolonged therapy over several weeks to months as compared to short courses used to treat cutaneous infections. At the present time, doxycycline and minocycline are the most commonly prescribed tetracyclines in dermatology, used primarily for treatment of acne vulgaris with a long overall favorable track record of effectiveness and safety. Although both are commonly used, doxycycline may be chosen by clinicians more readily as there is a lower risk of rare yet potentially serious adverse reactions, although doxycycline does warrant preventative measures to reduce the risks of esophagitis and phototoxicity reactions. This article reviews data with a new double-scored small 150mg tablet of doxycycline hyclate that has proven functional scoring, exhibits bioavailability similar to enteric-coated doxycycline, and has been shown to be associated with a low potential for gastrointestinal adverse reactions very comparable to what is achieved with enteric-coated tablets. (*J Clin Aesthet Dermatol.* 2015;8(5):19–26.)

For approximately six decades, oral antibiotics have been used for the treatment of acne vulgaris (AV), primarily in patients with a predominance of inflammatory lesion involvement that is at least moderate in severity and/or in those who are poorly responsive to an adequate trial of topical therapy alone.[1,2] From the mid-1950s through the early 1970s, the predominant oral antibiotics that were utilized were tetracycline and erythromycin, with oral dapsone used selectively for treatment of severe recalcitrant nodular AV.[1–4] Over time, as the sensitivity of many strains of *Propionibacterium acnes* to erythromycin and tetracycline decreased, the therapeutic utility of these two agents also diminished, leading to increased use of two "newer generation" tetracyclines, doxycycline, released in 1967, and minocycline, released in 1971.[3,5–11] To add, both doxycycline and minocycline offered the advantages of less frequent daily dosing, greater lipophilicity than tetracycline, and a

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lower potential for food-drug interactions.[10,11] The greater lipophilicity of doxycycline and minocycline is believed to directly correlate with drug penetration into the lipid-rich pilosebaceous unit, which is an important target site in AV.[10,11]

The widespread global use of oral antibiotics for AV (especially tetracyclines) over several years brings to light the conspicuous lack of new systemic agents for the treatment of AV. With the exception of oral isotretinoin, which was a major breakthrough for severe nodular AV in the early 1980s, the development and emergence of new oral therapies for AV has been essentially nonexistent. Other than topically applied or ingested medications, the development of other types of treatment for AV has increased more recently, especially with physical modalities and devices. Unfortunately substantiation of efficacy by cogent scientific evidence with most of these therapeutic approaches and products has been limited.[2,12] As a result, oral antibiotic therapy continues to be an integral part of the therapeutic armamentarium for AV, including in published AV treatment guidelines, primarily for patients with moderate-to-severe disease, used in combination with topical therapy.[1,2,13,14] Nevertheless, considerations related to relative efficacy, side effects, concerns related to antibiotic resistance, and "access to medication" issues are important to address.

This article focuses primarily on doxycycline, which has been the most widely prescribed oral tetracycline agent in the United States, at least over the past few years. An overview of pharmacologic and therapeutic characteristics of doxycycline that relate to use for AV, with some comparative information with other tetracyclines, is summarized. Emphasis is placed on a new tablet formulation of doxycycline hyclate, including a review of studies completed with this agent, and a discussion of what this formulation may offer clinicians that is clinically relevant. Although formulations of subantimicrobial dose doxycycline will be mentioned when necessary for explanatory purposes, this article refers primarily to antibiotic dose doxycycline formulations (≥50mg).

HOW ARE DOXYCYCLINE AND MINOCYCLINE USED IN DERMATOLOGY?

Both doxycycline and minocycline are widely prescribed by dermatologists, most often for the treatment of AV, but are also used to treat other noninfectious inflammatory skin diseases such as rosacea, and a variety of cutaneous infections.[7,11] Data from 2011 showed that dermatologists in the United States prescribed 8,153,961 antibiotic prescriptions of which doxycycline and minocycline comprised 38 and 30 percent, respectively.[15] Based on this same database, 6,174,025 antibiotic prescriptions (75.7%) were written by US dermatologists for a tetracycline agent; the distribution of prescriptions among the tetracyclines was doxycycline hyclate (43%), immediate-release minocycline hydro-chloride (23%), extended-release minocycline tablets (15%), sub-antimicrobial dose doxycycline 40mg modified-release (MR) capsules (9%), tetracycline hydrochloride (6%), and doxycycline monohydrate (4%).[15] These data reflect the high level of dependence on the tetracycline class of antibiotics within dermatology, especially doxycycline and minocycline.[1,3–5,11]

WHAT CHARACTERISTICS SUPPORT THE TETRACYCLINE CLASS OF ANTIBIOTICS AS FAVORABLE FOR THE TREATMENT OF ACNE VULGARIS?

As mentioned above, the tetracyclines have been the most commonly used oral antibiotics for the treatment of AV, with doxycycline or minocycline currently being the two most frequent choices by clinicians in the United States based on widespread clinical experience over many years and multiple publications and studies that support both efficacy and favorable safety.[1,3,10,11] The major tetracycline antibiotics—tetracycline, doxycycline, and minocycline—have been approved by the US Food and Drug Adminstration (FDA) for the treatment of a broad range of infections since 1953, 1967, and 1971, respectively.[11] As mentioned above, the rationale for the more frequent use of doxycycline and minocycline as compared to tetracycline for treatment of AV include the apparent need for less frequent daily dosing, lower prevalence of less sensitive *P. acnes* bacterial strains, and greater lipophilicity than tetracycline.[10,11,16] In addition, both doxycycline and minocycline exhibit favorable long-term track records of efficacy and safety overall.[1–3,11] To add, tetracycline exhibits a greater decrease in gastrointestinal (GI) absorption when co-ingested with metal ions present in high concentrations in foods (i.e., milk, yogurt, fortified cereals), vitamin/mineral supplements, and antacids that contain calcium, magnesium, and/or aluminum.[17,18] All immediate-release minocycline formulations and all doxycycline formulations (other than subantimicrobial-dose doxycycline) are indicated for "adjunctive therapy for severe acne" as depicted in their FDA-approved product labeling (package inserts).[19–21] Extended-release minocycline tablets are approved for the treatment of inflammatory lesions in patients with non-nodular moderate-to-severe AV with the recommendation of weight-based dosing (1mg/kg/day).[22] Subantimicrobial-dose doxycycline is FDA approved for the treatment of papulopustular lesions of rosacea (doxycycline 40mg-MR capsule once daily), and as an adjunct to scaling and root planing to promote attachment level gain and to reduce pocket depth in patients with adult periodontitis (doxycycline hyclate 20mg twice daily).[23] A daily dose of ≥50mg of doxycycline hyclate or monohydrate ≥50mg represents antibiotic-dose doxycycline due to the potential to exhibit continuous antibiotic selection pressure, and is clearly distinct from subantimicrobial-dose doxycycline.[24]

WHAT FACTORS DIFFERENTIATE DOXYCYCLINE AND MINOCYCLINE FOR THE TREATMENT OF ACNE VULGARIS?

Although a complete review and differentiation of doxycycline and minocycline is beyond the scope of this

article, information has been reviewed in detail elsewhere.[10,11,25,26] Suffice it is to say, both are commonly prescribed for treatment of AV, both are often effective, and each exhibits some unique pharmacological properties that may prove to be potentially advantageous and/or disadvantageous in some cases. The following reviews a few areas of differentiation between doxycycline and minocycline.

Phototoxicity. Minocycline exhibits negligible photosensitivity while doxycycline exhibits dose-related phototoxicity.[11,27] Although dose-related comparative data with doxycycline are limited, a case analysis from the United Kingdom of 106 acne patients evaluated over a two-year period reported sunburn-like phototoxicity in 20 percent of patients (6/30) treated with doxycycline 150mg/day and 42 percent of patients (32/76) treated with doxycycline 200mg/day.[28] In all cases, extended sun exposure was associated with the sunburn reaction, with the vast majority experiencing the reaction while on vacation. Approximately one-third continued doxycycline, allowing the reaction to lessen over the following weeks with avoidance of high levels of sun exposure. The visible erythema on sun-exposed skin and associated symptoms resolved over 10 to 14 days in almost all cases, with two patients reporting persistent skin soreness, which resolved within one month. None of the patients developed persistent sequelae, such as scarring or dyschromia. The authors suggested that a dose-related phenomenon exists with doxycycline, and that the risk is associated with a time period of more intense sun exposure as phototoxic reactions to doxycycline require a threshold of light exposure to occur, which can be mitigated by broad spectrum sunscreen use. Preventative measures are to be followed more diligently in patients taking doxycycline when it is known or anticipated that greater intensity of ultraviolet (sun) exposure will be occurring.

Vestibular side effects. Vestibular side effects, such as vertigo and dizziness, are not characteristic side effects associated with doxycycline use.[1,3,4,16] Although both minocycline and doxycycline are lipophilic, the greater lipophilicity of minocycline supports the theoretical advantage of higher levels of penetration into the pilosebaceous "target site" in AV, although quantitative methods to measure follicular drug concentrations are not currently available.[10,11] The down side of higher lipophilicity with minocycline as compared to other tetracyclines is greater passage through the blood brain barrier. This leads to penetration into the vestibular apparatus of the ear, which can cause troublesome dizziness and vertigo in some patients treated with minocycline, reported especially with immediate-release formulations, especially some generic products.[1–4,11,25] Minocycline-associated vertigo usually becomes evident after the first dose or within the first few doses, which allows discontinuation of therapy should this side effect occur. To add, although proper weight-based dosing of the extended-release minocycline formulation does not completely eliminate vertigo/dizziness as a potential side effect, dosing at 1mg/kg/day has been shown to reduce acute vestibular side effects when compared to higher daily doses (2mg/kg/day or 3mg/kg/day) without overall differences in efficacy.[26]

Efficacy comparisons. Although both minocycline and doxycycline have a long overall track record of widespread use with well-recognized efficacy, and safety when used to treat AV, prescription tracking data as depicted above has more recently shown that doxycycline is most commonly prescribed by dermatologists, followed by immediate-release minocycline formulations and extended-release minocycline tablets.[15] Several factors may account for trends in prescribing patterns over various time periods, including cost-related factors, third-party coverage and access, efficacy and/or safety concerns, and brand-related marketing strategies. Although there was suggestion in the past that minocycline is more efficacious than doxycycline for AV, there is no strong scientific evidence to state that either agent is superior to the other in efficacy, and there is no comparative evidence with treatment of AV between any formulation of doxycycline and weight-based dosing with extended-release minocycline tablets.[29,30] To add, both agents exhibit a variety of anti-inflammatory properties unrelated to their antibiotic activity that may contribute to their efficacy with AV treatment.[31,32]

Other adverse reactions. In scrutinizing these agents, one factor that may directly affect the prescribing choice among many clinicians is the possibility of rare but potentially serious adverse effects that have been reported with minocycline and are very unlikely or nonexistent with doxycycline. These include drug-associated lupus-like syndrome, autoimmune hepatitis, and drug hypersensitivity syndrome with associated systemic manifestations (i.e., hepatitis, pneumonitis), in addition to other minocycline-specific side effects, such as vertigo/dizziness and patterns of cutaneous and/or mucosal hyperpigmentation.[1–4,11,25,33–39] The major side effect concerns among dermatologists that are associated with use of doxycycline are GI side effects (i.e., esophagitis) and dose-related photosensitivity, both of which can usually be averted by preventative measures.[1–4,11,25,27,28,40,41] It is important to emphasize that minocycline has been used extensively for more than four decades and that serious side effects are rare. Nevertheless, the balancing of several factors as mentioned above and the overall comparison of side effect profiles has resulted in a general trend toward more common prescribing of doxycycline. Such prescribing trends can vary over time and change quickly based on the influence of several factors, such as intermittent drug shortages from manufacturers, rising costs of some generic formulations, relative quantity of available branded formulations, new scientific data on efficacy and/or safety related to specific products/ formulations, marketing programs by specific brands, and availability of reliable and efficient drug access programs.

WHAT IS THE CLINICAL RELEVANCE OF ORAL DOXYCYCLINE FORMULATIONS?

GI side effects, including "pill esophagitis," are perhaps

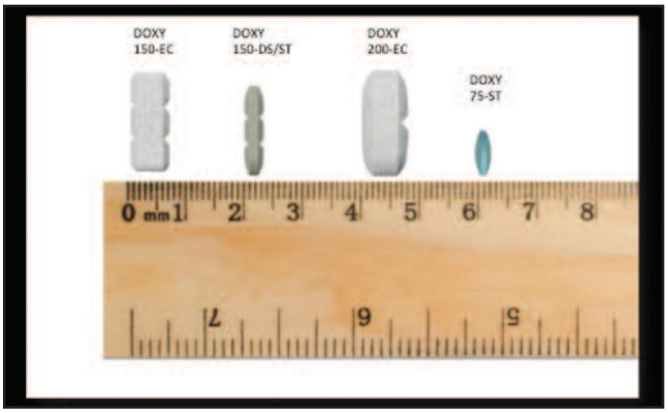

Figure 1. Tablet size comparisons of brand doxycycline hyclate formulations

DOXY 150-EC—Doxycycline hyclate 150mg Enteric-Coated Tablet;
DOXY 150-DS/ST—Doxycycline hyclate 150mg Double-Scored Small Tablet;
DOXY 200-EC—Doxycycline hyclate 200mg Enteric-Coated Tablet;
DOXY 75-ST—Doxycycline hyclate 75mg Small Tablet

the most common concerning side effect associated with the use of oral doxycycline.[11,25,34,40,41] Although it has been stated that GI side effects are more common with the hyclate salt than monohydrate salt of doxycycline, this suggestion is not adequately supported by scientific data including clinical studies in humans, and was based on study data using monkey esophagus and reported differences in pH.[11,34] On the contrary, to date, studies with enteric-coated formulations that delay the release of doxycycline so that the majority of the active drug bypasses gastric exposure have shown a quantitative reduction in GI side effects as compared to an immediate-release doxycycline formulation available at the time the studies were completed.[42,43]

Most recently, a branded, double-scored 150mg small tablet formulation of doxycycline hyclate (doxy 150-DS/ST) has been released into the marketplace (Acticlate 150mg, Aqua Pharmaceuticals, West Chester, Pennsylvania), along with a 75mg non-scored tablet under the same brand (Acticlate 75mg, same company). Each doxy 150-DS/ST can be broken at both scores into thirds, with each of the one-third segments containing 50mg. Another option based on dosing needs in a given patient is that one score can be broken, leaving a two-third tablet containing 100mg and a one-third tablet containing 50mg. If a single dose of 150mg is desired, the entire doxy 150-DS/ST can be ingested with a full glass of water, especially as the very small tablet size facilitates swallowing, especially by patients who have difficulty ingesting larger tablets or capsules (Figure 1). Discussed below are the results of studies that evaluate the bioavailability of doxy 150-DS/ST when ingested with and without food and also a comparison of the potential for GI side effects between doxy 150-DS/ST and enteric-coated doxycycline hyclate tablets.

EVALUATION OF CRITERIA FOR TABLET SCORING

It has been noted that tablet splitting may not always produce tablet segments that are stable or that contain an acceptably equal amount of active ingredient in each segment.[44] In addition, tablet size is an important factor affecting the ability of some patients to completely swallow medication.[45] The double-scored tablets of doxy 150-DS/ST were developed to meet all recommended criteria provided in the March 2013 FDA guidance for functional scoring entitled "Tablet Scoring: Nomenclature, Labeling, and Data for Evaluation."[46] These include multiple tests to demonstrate (1) a loss of mass of <3.0 percent between at least 45 individual tablet segments, (2) confirmation that the split-tablet segments meet the United States Pharmacopeia Friability requirement, (3) demonstration of dissolution data on split-tablet portions that meet finished-product release requirements, (4) proof of adequate stability of split tablets stored in pharmacy dispensing containers for a period of 90 days under designated temperature conditions, (5) analyses showing that split-tablet segments meet the finished-product testing requirements relative to their dosage size and content, and (6) uniformity test data of the tablet segments to demonstrate that the content uniformity criteria are met using both tablet mass and assay methods. The 90-day shelf life study was performed on tablets split both mechanically, using a tablet splitter device, and manually. All split tablet segments, regardless of splitting methodology, met the drug product specification criteria discussed above for their proportional size (50mg).[47]

The content analysis of each segment is important to clinicians who sometimes wonder if splitting tablets produces an accurate quantity of active ingredient in each tablet segment. *In following a designated protocol to determine uniformity of dosage units, if specified criteria are met, the formulation can claim to exhibit functional scoring.*[46] Using a typical 150mg tablet lot of doxy 150-DS/ST, 10 tablets were split into 30 segments (10-left, 10-middle,10-right) with each segment assayed for the amount of doxycycline contained in the tablet segment. Tablet uniformity testing after breaking the 10 complete double-scored tablets into 30 individual segments showed a range from 49.7mg to 50.3mg among the left, middle, and right segments. These results confirmed that doxy 150-DS/ST tablets exhibit functional scoring, indicating that when tablets are split at their scores, each tablet segment provides a dose of 50mg.[47]

BIOAVAILABILITY STUDY (STUDY 1)

Methodology. A single-dose, randomized, two-treatment, two-period, two-sequence, crossover study was completed to evaluate the relative bioavailability of doxy-150-DS/ST under fasted (N=26) and non-fasted (N=25) conditions in healthy volunteer subjects.[47] In one study period, a single tablet of doxy 150-DS/ST was administered after an overnight fast of ≥10 hours. In the other study period, a single tablet of doxy 150-DS/ST was administered to the same subjects following a

standardized 1000-calorie, high-fat meal (breakfast), which is the specified food intake used with pharmacokinetic testing of lipophilic drugs that are not highly water soluble. This high calorie-high fat meal included two fried eggs (in butter), bacon (2 strips), hash brown potatoes (4 ounces), buttered toast (2 slices), and a glass of whole milk (8 ounces). The order of administration either with or without food was randomized using a two-sequence schedule. All subjects were sequestered at the study facility from at least 10.5 hours before administration of the study drug and until after the 24-hour blood collection. All subjects then returned to the study facility for pharmacokinetic blood sampling at 36 hours, 48 hours, and 72 hours. The interval between study drug administration in the two distinct study periods was 14 days. Blood samples were collected at pre-dose and at intervals over 72 hours after dosing in each period. The plasma samples from all subjects who completed the study were shipped according to the proper standards for specimen handling to the reference laboratory approved in the study protocol.

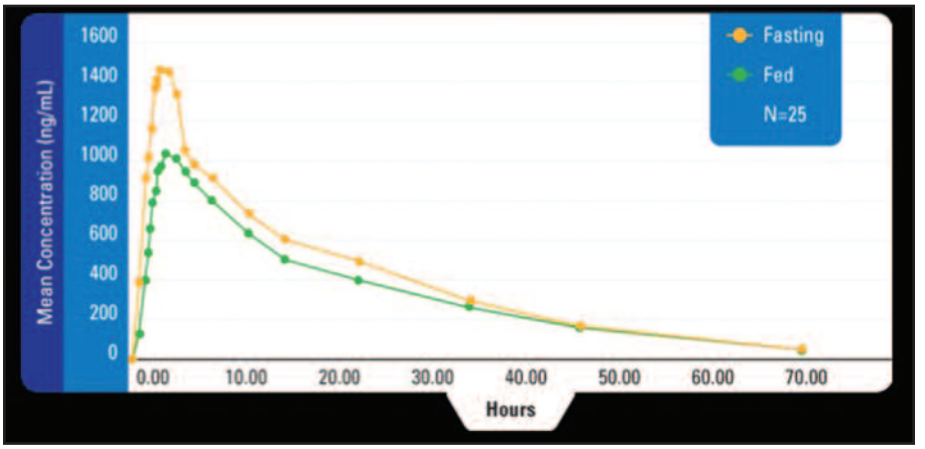

Figure 2. Bioavailability comparison of doxycycline hyclate 150mg double-scored small tablet in fed versus fasted state. Randomized, single-dose, two-period, two sequence crossover study

Adverse Event	Treatment[1]	
	FED STATE	FASTED STATE
	N[2] = 25	N = 26
	n[3] (%[4])	n (%)
Abdominal discomfort	0 (0.0)	2 (7.69)
Abdominal pain	0 (0.0)	1 (3.85)
Diarrhea	0 (0.0)	1 (3.85)
Nausea	0 (0.0)	2 (7.69)

Figure 3. Doxycycline hyclate 150mg double-scored small tablet comparison of gastrointestinal adverse events in fed versus fasted state. Randomized, single-dose, two-period, two sequence crossover study

Statistical analysis using average bioequivalence methodology was performed to evaluate the relative bioavailability of the test formulation when taken after food ingestion (standardized high calorie-high fat meal) compared to when taken in the fasted state. The effect of food was determined based on the confidence intervals for major pharmacokinetic (PK) parameters for doxycycline, which were log transformed. These major PK evaluations were assessments of area-under-the-curve (AUC) parameters ($AUC_{0\text{-}t}$, $AUC_{0\text{-}inf}$) and maximum serum concentration (Cmax). The effect of food on doxy 150-DS/ST was based on the log-transformed data by comparing Test A (fed sate) results versus Reference B (fasted state) results. If the 90-percent confidence intervals for the test/reference ratio for $AUC_{0\text{-}t}$, $AUC_{0\text{-}inf}$, and Cmax for doxycycline all fell within the range of 80 to 125 percent in the fed state compared to the fasted state, it was then concluded that concurrent food ingestion produced a negligible to no effect on the bioavailability of the doxy 150-DS/ST.

Study outcomes using the above methodology showed that Cmax was reduced by approximately 24 percent compared with the fasted state, but the median Tmax remained the same (2.25 hours). The overall bioavailability as measured by AUC was decreased by about 15 to 18 percent when doxycycline hyclate tablet was administered after a high-fat meal compared to administration in the fasted state. The bioavailability outcome evaluating mean plasma concentrations in the fed versus fasted state are depicted in Figure 2. This relatively modest reduction in doxycycline bioavailability associated with concurrent food ingestion is consistent to what has been observed with doxycycline and other tetracyclines.[10,11] As the treatment of AV is more dependent on repeated administration over a period of several weeks to months, this modest decrease in maximum systemic exposure demonstrated after administration of a single dose with food high in fat content is not felt to be clinically relevant overall with respect to efficacy, especially in a select group of patients

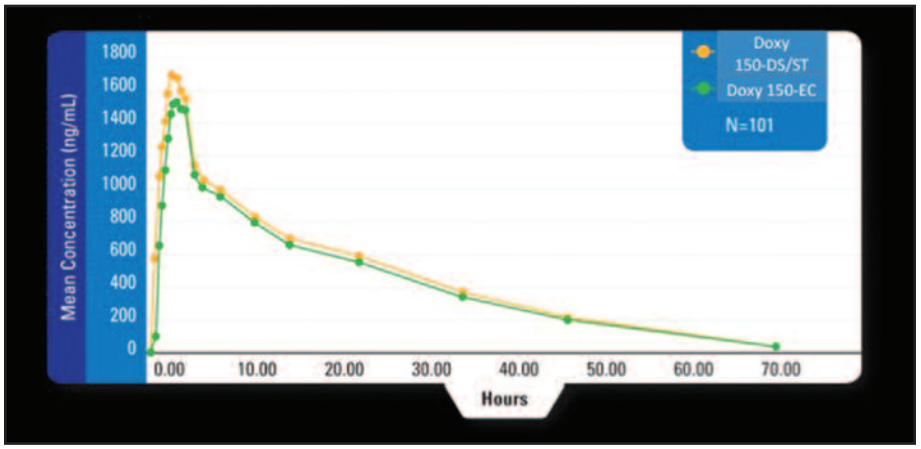

Figure 4. Bioavailability comparison in fasted state of doxycycline hyclate 150mg double-scored small tablet (Doxy 150-DS/ST) versus doxycycline hyclate 150mg enteric-coated tablet (Doxy 150-EC). Randomized, single-dose, two-period, two sequence crossover study

Body System/Adverse Event	Bioequivalence Study	
	Doxy 150-DS/ST	Doxy 150-EC
	N (%)	N (%)
Gastrointestinal disorders		
Abdominal pain	1 (0.92%)	2 (1.92%)
Diarrhea	1 (0.92%)	0 (0.00%)
Dyspepsia	1 (0.92%)	0 (0.00%)
Nausea	4 (3.67%)	10 (9.62%)
Vomiting	1 (0.92%)	0 (0.00%)

Figure 5. Comparison of gastrointestinal adverse events in fasted state of doxycycline hyclate 150mg double-scored small tablet (Doxy 150-DS/ST) versus doxycycline hyclate 150mg enteric-coated tablet (Doxy 150-EC). Randomized, single-dose, two-period, two sequence crossover study

who may tolerate the medication better when administered with food.

Safety assessments. GI-related adverse events (AEs) are the most significant safety consideration with doxycycline use, especially with a single-dose study. In this study, administration without food resulted in 6/26 patients experiencing GI-related AEs (nausea 2; abdominal discomfort 3; diarrhea 1). The majority of AEs were rated as mild in severity. Administration of doxy 150-DS/ST with the designated food intake at breakfast in the same subject population (minus one subject who did not follow up for the second study part) was not associated with any GI side effects (Figure 3).

Study summary. The bio-availability of doxy 150-DS/ST was modestly reduced by concurrent ingestion with a high calorie-high fat meal at breakfast as compared to the fasted state (empty stomach). Many patients may be able to ingest doxy 150-DS/ST with a large glass of water without concomitant food intake and not experience GI side effects. However, as is consistent with doxycycline formulations in general, administration with food along with ingestion concurrently with a good volume of water or an appropriate liquid (~8 ounces) reduces the overall risk of GI-related side effects.[1–3,10,11]

COMPARATIVE BIOAVAILABILITY AND SAFETY/TOLERABILITY (STUDY 2)

Methodology. A single-dose, randomized, two-treatment, two-period, two-sequence, crossover study, with the same two study period timing as Study 1, was completed comparing the bioavailability of doxy 150-DS/DT (N=109) and a branded doxycycline 150mg enteric-coated tablet (doxy 150-EC; N=104). Both study drugs were administered in the fasted state in order to assess GI-related AEs (side effects) without the influence of concurrent ingestion with food. Collectively, 112 subjects were en-rolled with 101 subjects completing both study phases.[47]

Bioavailability outcomes. The bioavailability profiles of the two doxycycline formulations were very similar. Figure 4 depicts mean plasma concentrations of both agents over time.

Safety/tolerability outcomes. The safety/tolerability profiles with both agents were also similar with focus on GI-related AEs (Figure 5). When study subjects received doxy 150-DS/ST (N=109), eight GI-related side effects were reported (nausea 4, vomiting 1, abdominal pain 1, diarrhea 1, dyspepsia 1), with one of the subjects who experienced nausea also reporting vomiting and abdominal pain. Therefore, 6/109 subjects experienced GI-related side effects after ingestion of doxy 150-DS/ST. In the study phase where subjects took doxy 150-EC (N=104), 12/104 subjects experienced GI-related side effects (nausea 10, abdominal pain 2). No other major safety signals emerged during the study.

Study summary. Doxy 150-DS/ST and doxy 150-EC exhibited similar bioavailability after single-dose administration in the fasted states. The GI-related AE profile was also similar between the two drugs, with nausea being the most common side effect observed with both agents. In the doxy 150-DS/ST study phase, 6/109 subjects experienced GI-related side effects. It is important to note that both study drugs were administered in the fasted state

to maximize challenge of their respective potentials to produce GI side effects.

CONCLUSION

Both doxycycline and minocycline are commonly used to treat moderate-to-severe inflammatory AV. Doxycycline prescribed at an antibiotic dose exhibits favorable efficacy and safety and may be used somewhat more frequently than minocycline in dermatology due to a lower risk with doxycycline of rare yet potentially severe AEs that are idiosyncratic and cannot be averted by preventative measures. Nevertheless, both doxycycline and minocycline remain widely prescribed based on decades of clinical experience and published literature with treatment of AV. Each agent exhibits potential advantages in specific clinical situations and with individual patients affected by AV.

The recent availability of a new double-scored small tablet branded formulation of doxycycline hyclate (doxy 150-DS/ST) has been shown to exhibit only a modest reduction in bioavailability when ingested with a high calorie-high fat meal. In addition, the bioavailability of doxy 150-DS/ST is essentially the same as a brand doxycycline enteric–coated formulation (doxy 150-EC), with both formulations associated with a similar risk of GI-related side effects, including when administered in the fasted state. In fact, from a nominal perspective, the number of subjects experiencing GI-related side effects was slightly lower when the same study subjects ingested the doxy 150-DS/ST. The small tablet size of doxy 150-DS/ST facilitates ingestion especially in individuals who have difficulty swallowing solid medications. The double scoring of the 150mg tablet size allows for dosage adjustment by the clinician, with each of the three sections of the doxy 150-DS/ST tablet shown to contain 50mg in specific analytical studies, thus achieving the designated claim of functional scoring. If access to this formulation is available through third-party coverage and/or support programs to reduce the cost to the patient, available data supports doxy 150-DS/ST as a very good addition to the oral antibiotic armamentarium in dermatology.

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