Review of Mechanisms of Release of Commonly Prescribed Tetracyclines

Pearl Kwong MD, PhD, FAAD [a], Hilary Baldwin MD, FAAD [b], Debbie Glaab MSN, CPNP-AC [c], Rhonda Schreiber MS, RN [c], Emma Hignett BS [d]

INTRODUCTION

Dermatologists prescribe more oral antibiotics than any other specialty.[1] From the mid-1950s to the early 1970s, the predominant oral antibiotic utilized to treat inflammatory skin disease was tetracycline.[2] Since then, there has been increased use of three newer generation tetracyclines. Doxycycline was introduced in 1967, minocycline in 1971, and most recently sarecycline in 2018.[2,11] These are available in various mechanisms of release (MOR). The most common MORs used in dermatology are immediate release (IR), delayed release (DR), and extended release (ER). While clinicians prescribe all these MORs, there is a lack of synthesized information regarding their impact on clinical considerations for use. The data presented here is intended to increase clinician understanding of MORs, provide a quick reference source, and support individualized patient care.

OBJECTIVE

- To create a resource regarding the MOR of oral tetracyclines used in dermatology.

METHODS

- A systematic literature search of peer-reviewed publications was conducted over a 25-year period
- The primary focus of the review was to summarize differences between IR, ER, and DR and examine them pharmacologically and clinically
- Data was summarized into tabular format for ease of reference

RESULTS

Sixteen publications related to MOR were identified from this review. Consistently, the tetracycline derivatives doxycycline and minocycline were the most frequently used to treat inflammatory skin disease with a long and favorable track record of effectiveness and safety.[2] Although newer and with fewer publications, sarecycline was shown to be both efficacious and safe in treating acne vulgaris.[11] Currently doxycycline is available in both immediate and delayed-release formulations, minocycline in immediate and extended release, and sarecycline in immediate release. Delayed and extended release formulations were developed to address tolerance issues, achieve desired therapeutic objectives, and improve patient compliance concerns identified with the original immediate release formulations.[4] All 3 MORs have value in treatment regimens and may improve patient outcomes when fully understood and utilized in a manner that maximizes their formulation benefits to meet individual needs. Table 1 below provides a quick reference regarding MOR for the currently available branded tetracycline products.

Figure 1: Mechanisms of Release

IR formulations release most of the active drug very quickly after oral administration.3

DR formulations are enteric coated, allowing most of the active drug to bypass the upper GI tract.[2]

ER formulations release active drug over a longer period of time to provide stabilized pharmacodynamic effect.[5]

Table 1: MOR Quick Reference

	Immediate Release	Delayed Release	Extended Release
Considerations for treatment	• Active drug released in stomach absorbed in small intestine[3,4] • Intended to achieve rapid onset of pharmacodynamic effect[4] • Can also induce or exacerbate GI side effects[8] and vestibular side effects (Minocycline only)[4,5,17] • Impact of food and dairy varies among IR products and prescribing information should be checked prior to dosing[9,10,11,15,16,17]	• Active drug released and absorbed in the small intestine[2,4] • Intended to reduce side effects related to upper GI tract exposure[4] • Can take with or without food[12,13] • Can take with dairy[12,13]	• Active drug released in the stomach and absorbed in small intestine[4,5] • Intended to reduce systemic side effects and allow for less frequent dosing [4, 5] • Longer half-life with more consistent systemic exposure[5] • Can take with or without food[14,15,16] • Impact of dairy varies among ER products and prescribing information should be checked prior to dosing[14,15,16]
Examples	• Doxycycline hyclate (Targadox®, Acticlate®)[9,10] • Sarecycline (Seysara®)[11] • Minocin® (minocycline hydrochloride)[17]	• Doxycycline hyclate (Doryx®)[12] • Doxycycline hyclate modified polymer coating (Doryx® MPC)[13]	• Minocycline HCL (Solodyn®)[14] • Minocycline hydrochloride (Minolira™)[15] • Minocycline hydrochloride (Ximino™)[16]

CONCLUSIONS

This review highlights the evolution of oral formulations of tetracyclines most prescribed in dermatology. Distinct differences, based on MOR, have been noted in literature regarding reduction in some side effects and administration.[4,5] Tolerability and ease of use, as suggested by MOR, have been correlated to improved compliance with treatment regimens.[6,7] The data suggests that understanding the MOR of tetracyclines may be an important consideration to guide individualized treatment and improve patient outcomes. The data reviewed demonstrates that these different mechanisms of release have unique side effect profiles and considerations for treatment which may impact tolerability, patient preference, and compliance with treatment regimens.[8]

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1.Barbieri JS, Bhate K, Hartnett KP, Fleming-Dutra KE, Margolis DJ. Trends in Oral Antibiotic Prescription in Dermatology, 2008 to 2016. JAMA Dermatol. 2019;155(3):290–297. doi:10.1001/jamadermatol.2018.4944. 2. Del Rosso JQ. Oral Doxycycline in the Management of Acne Vulgaris: Current Perspectives on Clinical Use and Recent Findings with a New Double-scored Small Tablet Formulation. J Clin Aesthet Dermatol. 2015;8(5):19-26. 3. Neeraj, Bhandari, et al. A Review on Immediate Release Drug Delivery System. Int. Res J Pharm. App Sci., 2014; 4(1):78-87. 4. Shargel, L., Wu-Pong, Susanna, Yu, A.B.C. (2012). Applied Biopharmaceutics & Pharmacokinetics, 6e. McGraw-Hill Education5. Torok HM. Extended-release Formulation of Minocycline in the Treatment of Moderate-to-severe Acne Vulgaris in Patients Over the Age of 12 Years. J Clin Aesthet Dermatol. 2013;6(7):19-22. 6. Moore A, Ling M, Bucko A, Manna V, Rueda MJ. Efficacy and Safety of Subantimicrobial Dose, Modified-Release Doxycycline 40 mg Versus Doxycycline 100 mg Versus Placebo for the treatment of Inflammatory Lesions in Moderate and Severe Acne: A 7. Randomized, Double-Blinded, Controlled Study. J Drugs Dermatol. 2015;14(6):581-586. 8. Kircik, L., Bikowski, J. Oral Formulations Optimizing outcomes and enhancing adherence through formulation advancements. Supplement to Practical Dermatology, December 2010. 9. TARGADOX® (doxycycline hyclate USP) (2020, July). Prescribing Information. Scottsdale, AZ, USA: Journey Medical Corporation. 10. ACTICLATE® (doxycycline hyclate) (2017, Oct). Prescribing Information. Winchester, KY, USA: Catalent Pharma Solutions. 11. SEYSARA® (sarecycline) (2020, Jun). Prescribing Information. Exton, PA, USA: Almirall LLC. 12. DORYX® (doxycycline hyclate) (2015, Aug). Prescribing Information. Greenville, NC, USA: Mayne Pharma, Inc. 13. Doryx® MPC (doxycycline hyclate delayed-release tablets) (2020, Jun). Prescribing Information. Greenville, NC, USA: Mayne Pharma, Inc. 14. SOLODYN® (minocycline HCl) (2017, July). Prescribing Information. Bridgewater, NJ, USA: Valeant Pharmaceuticals North America LLC. 15. Minolira™ (Minocycline hydrochloride) extended release) (2018, June). Prescribing Information. Charleston, SC, USA: EPI Health, LLC. 16. XIMINO™ (minocycline hydrochloride) extended-release capsules. (2017, April). Prescribing Information. Cranbury, NJ, USA: Sun Pharmaceutical Industries, Inc. 17. Minocin® (minocycline hydrochloride) Pellet-Filled Capsules , (2010, Aug). Prescribing Information. Cranford, NJ. USA: Triax Pharmaceuticals, LLC.

AFFILIATIONS

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