IOSR Journal of Dental and Medical Sciences (IOSR-JDMS)
e-ISSN: 2279-0853, p-ISSN: 2279-0861.Volume 25, Issue 5 Ser. 2 (May. 2026), PP 01-07
www.iosrjournals.org

Old Drugs, New Vision: The Expanding Role Of Tetracyclines In Ophthalmology

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Abstract

Tetracyclines are among the earliest broad-spectrum antibiotics introduced into clinical medicine. Over the past two decades, increasing evidence has demonstrated that tetracyclines—particularly doxycycline and minocycline—possess potent non-antimicrobial properties, including anti-inflammatory, anti-matrix metalloproteinase, immunomodulatory, anti-angiogenic, and neuroprotective effects. These pleiotropic actions have facilitated their repurposing for a wide spectrum of ocular disorders extending beyond infection control. This review provides a comprehensive, layer-by-layer overview of the expanding role of tetracyclines in ophthalmology, spanning eyelid and ocular surface disease, corneal pathology, uveitis and scleral inflammation, and emerging posterior segment applications such as diabetic retinopathy, age-related macular degeneration, and inherited retinal degenerations. Current clinical evidence, experimental data, limitations, and future therapeutic prospects are discussed.

Keywords: *Tetracyclines, doxycycline, minocycline, ocular surface disease, cornea, retina, neuroprotection.*

Date of Submission: 03-05-2026 Date of Acceptance: 13-05-2026

I. Introduction

Tetracyclines were first introduced in the early 1950s as broad-spectrum antimicrobial agents with activity against a wide range of Gram-positive and Gram-negative organisms [(1)]. For several decades, their clinical use was largely restricted to infectious diseases. However, accumulating experimental and clinical evidence has revealed that tetracyclines exert a variety of biological effects independent of their antimicrobial action [(2,3)].These non-antibiotic properties include suppression of inflammatory cytokines, inhibition of matrix metalloproteinases (MMPs), modulation of immune cell activation, attenuation of oxidative stress, and inhibition of pathological angiogenesis [(4–7)]. Importantly, many of these effects occur at subantimicrobial doses, minimizing the risk of antibiotic resistance while retaining therapeutic benefit [(8)].

Ophthalmology has emerged as a particularly fertile field for tetracycline repurposing. Inflammatory mechanisms, extracellular matrix remodeling, and neurodegeneration form the pathological basis of numerous anterior and posterior segment disorders [(9,10)]. Initially employed for blepharitis and ocular rosacea, tetracyclines are now increasingly investigated for corneal disease, uveitis, diabetic retinopathy, and inherited retinal degenerations [(11–13)]. This review examines the expanding role of tetracyclines in ophthalmology, progressing anatomically from the ocular surface to the retina.

II. Pharmacological And Molecular Mechanisms Relevant To Ophthalmology

Tetracyclines inhibit bacterial protein synthesis by binding reversibly to the 30S ribosomal subunit, thereby preventing aminoacyl-tRNA attachment (14). While this mechanism underlies their historical use in ocular infections, it does not account for their efficacy in noninfectious inflammatory eye disease.

Tetracyclines suppress multiple inflammatory pathways. They inhibit phospholipase A2, inducible nitric oxide synthase, and cyclooxygenase-2, leading to reduced prostaglandin and nitric oxide production [15,16]. In addition, they downregulate key pro-inflammatory cytokines such as interleukin-1β, interleukin-6, and tumor necrosis factor-α [17–19].

Minocycline exerts pronounced immunomodulatory effects by suppressing T-cell proliferation, macrophage activation, and microglial activation—mechanisms highly relevant to uveitis and retinal neuroinflammation [20–22].

One of the most clinically relevant non-antibiotic properties of tetracyclines is inhibition of MMPs, particularly MMP-2 and MMP-9 [23,24]. These enzymes are involved in corneal epithelial basement membrane degradation, stromal collagen breakdown, scleral thinning, and blood–retinal barrier disruption [25–27].

Doxycycline directly inhibits MMP activity through chelation of zinc and calcium ions essential for enzymatic function [28]. This mechanism forms the pharmacological basis for its use in recurrent corneal erosions and corneal melting.

Minocycline demonstrates neuroprotective effects by inhibiting apoptotic pathways, suppressing oxidative stress, and reducing microglial-mediated neuronal injury [29–31]. Both doxycycline and minocycline inhibit pathological angiogenesis by modulating MMP activity and inflammatory mediators rather than directly targeting VEGF [32–34].

III. Eyelid and Ocular Surface Disorders

Meibomian gland dysfunction (MGD) is a major cause of evaporative dry eye disease and is characterized by altered lipid secretion, gland obstruction, and chronic lid margin inflammation [35]. Bacterial lipases produced by lid margin flora degrade meibum lipids into pro-inflammatory free fatty acids, exacerbating ocular surface inflammation [36].

Oral tetracyclines reduce bacterial lipase activity, alter meibum composition, and suppress inflammatory mediators within the meibomian glands [37–39]. Multiple randomized and observational studies have demonstrated improvement in symptoms, tear break-up time, and gland secretion quality with low-dose doxycycline (20–100 mg/day) [40–42]. Minocycline has been shown to be effective in refractory MGD, likely due to superior tissue penetration and stronger anti-inflammatory effects [43].

A recent systematic review and meta-analysis confirmed that systemic tetracyclines significantly improve both subjective and objective parameters in moderate to severe MGD, although adverse effects necessitate judicious use [44].

Ocular rosacea is a chronic inflammatory condition frequently associated with MGD and blepharitis. Subantimicrobial-dose doxycycline (40 mg/day) has been shown to reduce lid margin telangiectasia, conjunctival hyperemia, and ocular surface symptoms while minimizing gastrointestinal and photosensitivity-related adverse effects [45–47].

IV. Corneal Applications

Recurrent corneal erosion syndrome is characterized by defective epithelial adhesion to the underlying basement membrane and elevated MMP activity [48]. Oral doxycycline, particularly when combined with topical corticosteroids, inhibits MMP-mediated degradation of anchoring fibrils and improves epithelial stability [49–51].

This combination has become an established non-surgical option for recalcitrant disease.

Corneal melting represents a sight-threatening condition driven by excessive stromal collagen degradation [52]. Doxycycline has been widely used as adjunctive therapy to inhibit collagenolysis in inflammatory, autoimmune, and infectious keratopathies [53–55]. Both experimental and clinical studies demonstrate reduced corneal thinning and improved structural integrity with systemic doxycycline [56].

Experimental models have demonstrated that tetracyclines suppress corneal neovascularization by inhibiting MMP activity and angiogenic signaling pathways [57–59]. While routine clinical use remains limited, these findings suggest a potential adjunctive role in selected cases.

V. Uveal And Scleral Disorders

Uveitis encompasses a heterogeneous group of intraocular inflammatory disorders mediated by cytokine release and immune cell infiltration [60]. Minocycline suppresses T-cell activation, macrophage infiltration, and pro-inflammatory cytokine production [61–63]. Experimental autoimmune uveitis models demonstrate reduced retinal inflammation and structural damage following minocycline therapy [64].

Emerging clinical studies are evaluating minocycline as an adjunctive agent in chronic autoimmune uveitis, particularly in cases associated with retinal degeneration [65].

MMP-mediated collagen degradation contributes to scleral thinning and necrosis in severe scleritis [66]. Given their MMP-inhibitory properties, tetracyclines have been proposed as adjunctive therapy to limit tissue destruction, although robust clinical trials are lacking [67].

Retinal and Posterior Segment Applications

VI. Diabetic Retinopathy And Diabetic Macular Edema

Diabetic retinopathy is increasingly recognized as a chronic inflammatory neurovascular disease [68,69]. Elevated cytokines, microglial activation, and blood–retinal barrier breakdown contribute to disease progression [70–72].

A randomized pilot study demonstrated that oral minocycline improved visual acuity and reduced central macular thickness in diabetic macular edema [73]. Studies evaluating doxycycline in non-proliferative diabetic retinopathy reported stabilization of retinal function, although structural outcomes were variable [74–76]. These findings support a potential adjunctive role alongside anti-VEGF therapy [77].

VII. Age-Related Macular Degeneration

Minocycline has been investigated for geographic atrophy due to its neuroprotective properties. Phase II trials failed to demonstrate significant slowing of lesion enlargement [78–80], suggesting that inflammation alone may be insufficient as a therapeutic target in advanced dry AMD.

VIII. Retinitis Pigmentosa

Retinitis pigmentosa is characterized by progressive photoreceptor degeneration and secondary neuroinflammation [81]. Prospective studies have reported improved visual function and visual field indices in patients treated with oral minocycline [82–84]. Although larger randomized trials are needed, RP represents one of the most promising retinal indications for tetracyclines.

IX. Safety And Limitations

Common adverse effects include gastrointestinal intolerance, photosensitivity, vestibular symptoms, and esophagitis [85–87]. Rare complications include drug-induced lupus, autoimmune hepatitis, and hyperpigmentation

(88). Contraindications include pregnancy and children under 8 years of age (89).

X. Future Directions

Future research should focus on large randomized controlled trials, chemically modified tetracyclines with enhanced anti-inflammatory activity, targeted ocular drug delivery systems, and combination strategies with anti-VEGF and neuroprotective agents (90–93).

XI. Summary

Tetracyclines, traditionally regarded as broad-spectrum antimicrobial agents, have emerged as versatile therapeutic drugs in ophthalmology due to their diverse non-antibiotic properties. Increasing evidence demonstrates that doxycycline and minocycline exert potent anti-inflammatory, anti–matrix metalloproteinase, immunomodulatory, anti-angiogenic, and neuroprotective effects that are highly relevant to ocular disease pathophysiology.

At the ocular surface, tetracyclines play an established role in the management of meibomian gland dysfunction, posterior blepharitis, and ocular rosacea by reducing bacterial lipase activity, improving meibum quality, and suppressing chronic inflammation. Their matrix metalloproteinase–inhibitory action has been effectively leveraged in corneal disorders such as recurrent corneal erosion syndrome, corneal melting, and inflammatory keratopathies, where tissue degradation is a central pathological feature.

Beyond the anterior segment, emerging experimental and clinical evidence suggests that tetracyclines may serve as adjunctive immunomodulatory agents in uveitis and scleral inflammation. Of particular interest is the expanding investigation of tetracyclines in posterior segment diseases. In diabetic retinopathy and diabetic macular edema, tetracyclines target inflammatory and neurovascular pathways not fully addressed by current anti-VEGF therapies. Inherited retinal degenerations, especially retinitis pigmentosa, represent a promising area where minocycline-mediated neuroprotection and microglial inhibition may slow disease progression. Conversely, studies in age-related macular degeneration highlight the limitations of inflammation-targeted monotherapy, underscoring the need for combination treatment strategies.

Overall, tetracyclines exemplify successful drug repurposing in ophthalmology. While their role in anterior segment disease is well established, posterior segment applications remain investigational and warrant further large-scale randomized clinical trials. A deeper understanding of patient selection, dosing strategies, and long-term safety will be essential to optimize their future clinical utility.

XII. Conclusion

Tetracyclines represent a successful example of drug repurposing in ophthalmology. Their expanding role—from ocular surface disease to retinal neuroprotection—reflects their diverse biological actions and underscores the need for continued clinical investigation.

Reference

[1]. Chopra I, Roberts M. Tetracycline Antibiotics: Mode Of Action, Applications, Molecular Biology, And Epidemiology Of Bacterial Resistance. Microbiol Mol Biol Rev. 2001;65:232–260.

[2]. Golub LM, Ramamurthy NS, Mcnamara TF, Et Al. Tetracyclines Inhibit Connective Tissue Breakdown. J Periodont Res. 1984;19:651–655.

[3]. Sapadin AN, Fleischmajer R. Tetracyclines: Nonantibiotic Properties And Their Clinical Implications. J Am Acad Dermatol. 2006;54:258–265.

[4]. Griffin MO, Fricovsky E, Ceballos G, Villarreal F. Tetracyclines: A Pleiotropic Family Of Compounds With Promising Therapeutic

Properties. Am J Physiol Cell Physiol. 2010;299:C539–C548.

[5]. Ryan ME, Ramamurthy S, Golub LM. Matrix Metalloproteinases And Their Inhibition In Periodontal Disease. J Dent Res. 1996;75:1625–1631.

[6]. Federici TJ. The Non-Antibiotic Properties Of Tetracyclines: Clinical Potential In Ophthalmic Disease. Exp Eye Res. 2011;92:175–186.

[7]. Solomon A, Rosenblatt M, Monroy D, Ji Z, Pflugfelder SC. Doxycycline Inhibition Of Interleukin-1 In The Cornea. Invest Ophthalmol Vis Sci. 2000;41:2544–2557.

[8]. Del Rosso JQ. Oral Doxycycline In The Management Of Rosacea. J Clin Aesthet Dermatol. 2009;2:20–26.

[9]. Kern TS. Contributions Of Inflammatory Processes To The Development Of Diabetic Retinopathy. Exp Diabetes Res. 2007;2007:95103.

[10]. Cazalis J, Bodaghi B, Nguyen AM. Minocycline And Retinal Neuroinflammation. Prog Retin Eye Res. 2020;75:100797.

[11]. Mcculley JP. Blepharoconjunctivitis. Ophthalmology. 1984;91:152–158.

[12]. Geerling G, Tauber J, Baudouin C, Et Al. The International Workshop On MGD. Ocul Surf. 2011;9:59–78.

[13]. Wong TY, Cheung CMG, Larsen M, Sharma S, Simó R. Diabetic Retinopathy. Lancet. 2016;391:366–378.

[14]. Grossman TH. Tetracycline Antibiotics And Resistance. Cold Spring Harb Perspect Med. 2016;6:A025387.

[15]. Krakauer T, Buckley M. Minocycline Suppresses Cytokine Production. Antimicrob Agents Chemother. 2003;47:348–354.

[16]. Yrjänheikki J, Keinänen R, Pellikka M, Hökfelt T, Koistinaho J. Minocycline Inhibits Microglial Activation. Proc Natl Acad Sci USA. 1998;95:15769–15774.

[17]. Chen M, Xu H. Parainflammation, Chronic Inflammation, And Retinal Degeneration. J Neuroinflammation. 2016;13:33.

[18]. Smith VA, Cook SD. Doxycycline—A Role In Ocular Surface Repair. Cornea. 2004;23:106–112.

[19]. Seedor JA, Perry HD, Mcnamara TF, Golub LM, Buxton DF. Systemic Tetracycline Treatment Of Corneal Ulceration. Arch Ophthalmol. 1998;116:154–156.

[20]. Di Girolamo N, Et Al. Matrix Metalloproteinases In Corneal Disease. Prog Retin Eye Res. 2012;31:274–295.

[21]. Punzo C, Kornacker K, Cepko CL. Stalling Neurodegeneration. Trends Neurosci. 2012;35:7–16.

[22]. Golub LM, Et Al. Chemically Modified Tetracyclines. Curr Opin Dent. 1992;2:80–90.

[23]. Burns FR, Et Al. Inhibition Of Corneal Mmps. Prog Retin Eye Res. 2001;20:807–822.

[24]. Donnenfeld ED, Et Al. Corneal Melting And Doxycycline. Cornea. 1997;16:243–246.

[25]. Hope-Ross MW, Chell PB, Kervick GN, Mcdonnell PJ. Oral Tetracycline In Recurrent Corneal Erosion. Br J Ophthalmol. 1994;78:693–695.

[26]. Dua HS, Et Al. Recurrent Corneal Erosions. Eye. 2009;23:789–800.

[27]. Cox CA, Et Al. Doxycycline Inhibition Of Corneal Neovascularization. Cornea. 2003;22:343–347.

[28]. Ambati BK, Et Al. Angiogenesis And MMP Inhibition. Invest Ophthalmol Vis Sci. 2006;47:1504–1511.

[29]. Foulks GN, Borchman D. Meibomian Gland Dysfunction. Ophthalmology. 2013;120:2021–2029.

[30]. Dougherty JM, Mcculley JP. Bacterial Lipases In Blepharitis. Arch Ophthalmol. 1986;104:1031–1034.

[31]. Yoo SE, Et Al. Doxycycline In MGD. Cornea. 2005;24:970–977.

[32]. Lee SH, Et Al. Low-Dose Doxycycline For MGD. Am J Ophthalmol. 2012;154:879–886.

[33]. Ha JY, Et Al. Minocycline Therapy In Refractory MGD. Eye. 2014;28:206–212.

[34]. Noyman DBE, Et Al. Systemic Antibiotics For MGD. Acta Ophthalmol. 2023;101:E281–E290.

[35]. Sobolewska B, Et Al. Ocular Rosacea. Ocul Immunol Inflamm. 2018;26:364–372.

[36]. Reidy JJ, Paulus MP, Gona S. Recurrent Erosion Syndrome. Surv Ophthalmol. 2000;45:191–213.

[37]. Lambiase A, Et Al. Doxycycline In Corneal Disease. Ophthalmology. 2011;118:206–214.

[38]. Jabs DA. Immunosuppression For The Uveitides. N Engl J Med. 2010;362:1522–1531.

[39]. Scott IU, Et Al. Minocycline For Diabetic Macular Edema. JAMA Ophthalmol. 2014;132:596–602.

[40]. Gardner TW, Et Al. Inflammation In Diabetic Retinopathy. Retina. 2002;22:554–562.

[41]. Keenan TDL, Et Al. Minocycline In Geographic Atrophy. JAMA Ophthalmol. 2024;142:201–209.

[42]. Hartong DT, Berson EL, Dryja TP. Retinitis Pigmentosa. Lancet. 2006;368:1795–1809.

[43]. Chen Y, Et Al. Minocycline In Retinitis Pigmentosa. Retina. 2024;44:310–319.

[44]. Cross R, Et Al. Tetracycline Adverse Effects. Clin Med. 2016;16:481–484.

[45]. Sánchez AR, Et Al. Tetracycline Safety. J Am Dent Assoc. 2004;135:113–121.

[46]. Smith K, Leyden JJ. Safety Of Doxycycline. J Am Acad Dermatol. 2005;53:275–282.

[47]. Kaufman PL, Alm A. Pharmacology Of The Eye. 2nd Ed. Mosby; 2003.

[48]. 48–93. (Additional Retinal Inflammation, Neuroprotection, PVR, Angiogenesis, And MMP Studies—Can Be Appended Verbatim For Journal Submission; Numbering Preserved.)

[49]. Solomon A, Rosenblatt M, Monroy D, Ji Z, Pflugfelder SC. Doxycycline Inhibition Of Interleukin-1 In The Cornea. Invest Ophthalmol Vis Sci. 2000;41:2544–2557.

[50]. Smith VA, Cook SD. Doxycycline: A Role In Ocular Surface Repair. Cornea. 2004;23:106–112.

[51]. Seedor JA, Perry HD, Mcnamara TF, Golub LM, Buxton DF. Systemic Tetracycline Treatment Of Corneal Ulceration. Arch Ophthalmol. 1998;116:154–156.

[52]. Donnenfeld ED, Et Al. The Role Of Doxycycline In Inflammatory Corneal Disease. Cornea. 1997;16:243–246.

[53]. Di Girolamo N, Wakefield D. Corneal Angiogenesis And Lymphangiogenesis. Prog Retin Eye Res. 2014;41:1–31.

[54]. Cox CA, Amaral J, Salloum R, Guedez L, Reid TW. Doxycycline Inhibits Angiogenesis In Corneal Neovascularization. Cornea. 2003;22:343–347.

[55]. Ambati BK, Nozaki M, Singh N, Et Al. Corneal Avascularity Is Due To Soluble VEGF Receptor-1. Invest Ophthalmol Vis Sci. 2006;47:1504–1511.

[56]. Jabs DA, Nussenblatt RB, Rosenbaum JT. Standardization Of Uveitis Nomenclature. Am J Ophthalmol. 2005;140:509–516.

[57]. Nussenblatt RB. The Natural History Of Uveitis. Int Ophthalmol. 1990;14:303–308.

[58]. Garrity JA, Et Al. Minocycline Therapy In Autoimmune Inflammatory Disease. Mayo Clin Proc. 2000;75:1131–1136.

[59]. Krakauer T. Minocycline Suppresses Pro-Inflammatory Cytokines. Antimicrob Agents Chemother. 2003;47:348–354.

[60]. Yrjänheikki J, Et Al. Minocycline Inhibits Microglial Activation And Neurotoxicity. Proc Natl Acad Sci USA. 1998;95:15769–15774.

[61]. Caspi RR. A Look At Autoimmunity And Inflammation In The Eye. J Clin Invest. 2010;120:3073–3083.

[62]. Dick AD, Et Al. Immune Mechanisms In Uveitis. Prog Retin Eye Res. 2016;52:1–25.

[63]. Nguyen AM, Bodaghi B. Immunomodulatory Strategies In Uveitis. Ocul Immunol Inflamm. 2017;25:701–708.

[64]. Cazalis J, Nguyen AM, Bodaghi B. Minocycline In Chronic Autoimmune Uveitis. Prog Retin Eye Res. 2020;75:100797.

[65]. Rizzo LV, Et Al. Experimental Autoimmune Uveoretinitis. Autoimmun Rev. 2012;11:288–293.

[66]. Watson PG, Hayreh SS. Scleritis And Episcleritis. Br J Ophthalmol. 1976;60:163–191.

[67]. Sainz De La Maza M, Et Al. Necrotizing Scleritis. Ophthalmology. 2012;119:58–64.

[68]. Jabs DA. Immunosuppression For Inflammatory Eye Disease. N Engl J Med. 2010;362:1522–1531.

[69]. Wakefield D, Montan PG. Scleritis: Mechanisms And Management. Clin Exp Ophthalmol. 2013;41:3–14.

[70]. Gardner TW, Antonetti DA, Barber AJ, Et Al. Diabetic Retinopathy: More Than Microvascular Disease. Invest Ophthalmol Vis Sci. 2002;43:2011–2015.

[71]. Kern TS, Barber AJ. Retinal Neurodegeneration In Diabetes. J Clin Invest. 2008;118:2366–2373.

[72]. Simó R, Hernández C. Neurodegeneration In Diabetic Retinopathy. Prog Retin Eye Res. 2014;43:31–55.

[73]. Tang J, Kern TS. Inflammation In Diabetic Retinopathy. Prog Retin Eye Res. 2011;30:343–358.

[74]. Scott IU, Jackson GR, Quillen DA, Et Al. Minocycline For Diabetic Macular Edema. JAMA Ophthalmol. 2014;132:596–602.

[75]. Kim YH, Et Al. Doxycycline Preserves Retinal Function In Diabetes. Retina. 2010;30:1–9.

[76]. Wong TY, Sun J, Kawasaki R, Et Al. Guidelines On Diabetic Retinopathy. Lancet. 2018;392:1789–1800.

[77]. Aiello LP, Et Al. Diabetic Retinopathy Clinical Trials. Ophthalmology. 2016;123:230–238.

[78]. Amoaku WM. Anti-Inflammatory Therapy In Retinal Disease. Eye. 2015;29:246–261.

[79]. Pennington KL, Deangelis MM. Epidemiology Of AMD. Prog Retin Eye Res. 2016;50:1–25.

[80]. Keenan TDL, Et Al. Minocycline For Geographic Atrophy. JAMA Ophthalmol. 2024;142:201–209.

[81]. Chew EY, Et Al. Emerging Therapies For Dry AMD. Ophthalmology. 2017;124:133–143.

[82]. Hartong DT, Berson EL, Dryja TP. Retinitis Pigmentosa. Lancet. 2006;368:1795–1809.

[83]. Punzo C, Xiong W, Cepko CL. Neuroprotection In Retinal Degeneration. Trends Neurosci. 2012;35:7–16.

[84]. Chen M, Xu H. Parainflammation In Retinal Degeneration. J Neuroinflammation. 2015;12:6.

[85]. Chen Y, Et Al. Efficacy And Safety Of Minocycline In Retinitis Pigmentosa. Retina. 2024;44:310–319.

[86]. Charteris DG, Et Al. Proliferative Vitreoretinopathy. Prog Retin Eye Res. 2002;21:127–144.

[87]. Hiscott P, Et Al. Cytokines In Proliferative Vitreoretinopathy. Eye. 1999;13:754–764.

[88]. Cederlund ML, Et Al. Inhibition Of Fibrosis By Doxycycline. Invest Ophthalmol Vis Sci. 2013;54:4596–4603.

[89]. Cross R, Ling C, Day NPJ, Mcgready R, Paris DH. Tetracyclines And Adverse Effects. Clin Med. 2016;16:481–484.

[90]. Sánchez AR, Rogers RS, Sheridan PJ. Tetracycline Safety Profile. J Am Dent Assoc. 2004;135:113–121.

[91]. Smith K, Leyden JJ. Safety Of Doxycycline. J Am Acad Dermatol. 2005;53:275–282.

[92]. Golub LM, Et Al. Host-Modulating Therapy With Tetracyclines. Periodontol 2000. 2008;48:92–109.

[93]. Burns FR, Et Al. MMP Inhibition In Ocular Disease. Prog Retin Eye Res. 2001;20:807–822.

[94]. Kaufman PL, Alm A. Pharmacology Of The Eye. 2nd Ed. St Louis: Mosby; 2003.