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FEATURES OF THE PATHOLOGY DEVELOPMENT OF HUMAN DEMODICOSIS. REVIEW

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Abstract

Relevance. Demodex is the most common parasite found on humans, and yet little is known about its pathogenicity in relation to the ocular surface. The growing interest in demodex over the past 20 years has expanded our understanding of this tick and its pathogenetic role. Despite the growing interest in demodex in the literature, numerous obstacles remain for future research, so the section of this review is devoted to identifying and proposing for future consideration. The lack of uniformity in terms of terminology, diagnostic methods and approach to the treatment of demodex remains an obstacle to future comparisons of studies. This review summarizes current knowledge about demodex and hopes to offer some recommendations for future directions in the study of demodex in humans.

Search strategy. The study examined full-text publications in English and Russian, which are devoted features of the pathology development of human demodicosis. In the process of searching for literature, the following search engines were used: Pubmed, Web of science, Cyberleninka, Google Scholar by keywords. The time period was designated 2007-2022. 299 publications were identified on this topic. Of these, 61 publications corresponded to the purpose of our study. Inclusion criteria: Publications of the level of evidence A, B: meta-analyses, systematic reviews, cohort and cross-sectional studies. Exclusion criteria: summary reports, newspaper articles and personal messages.

Results and conclusions. Papulopustular rosacea and demodecosis are common facial skin diseases that can be difficult to diagnose clinically. In addition to well-known clinical signs such as vascular signs and papules, in our study of patients with known papulopustular rosacea or demodecosis, we have shown that other clinical signs are also often present (inconspicuous follicular scales on the face, dandruff, folliculitis on the scalp, itching of the face or scalp). Therefore, the presence of these signs and symptoms should encourage dermatologists to conduct further diagnostic tests (for example, the recently described test based on the high density of demodex mites observed in these conditions) to ensure an accurate diagnosis.

Keywords: *demodex mite,ocular surface,inflammation.*

Резюме

ОСОБЕННОСТИ РАЗВИТИЯ ПАТОЛОГИИ ДЕМОДЕКОЗА ЧЕЛОВЕКА. ОБЗОР ЛИТЕРАТУРЫ

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Актуальность. Демодекс является наиболее распространенным паразитом, встречающимся у людей, и все же мало что известно о его патогенности по отношению к глазной поверхности. Растущий интерес к демодексу за последние 20 лет расширил наше понимание этого клеща и его патогенетической роли. Несмотря на растущий интерес к демодексу в литературе, для будущих исследований остаются многочисленные препятствия, поэтому раздел этого обзора посвящен выявлению и предложению для дальнейшего рассмотрения. Отсутствие единообразия с точки зрения терминологии, методов диагностики и подхода к лечению демодекса остается препятствием для будущих сравнений исследований. Этот обзор обобщает современные знания о демодексе и надеется предложить некоторые рекомендации для будущих направлений в изучении демодекса у людей.

Стратегия поиска. В исследовании изучены полнотекстовые публикации на английском и русском языках, которые посвящены особенностям развития патогенеза демодекоза человека. В процессе поиска литературы использованы следующие поисковые системы: Pubmed, Web of science, Cyberleninka, Google Scholar по ключевым

словам. Временной период был обозначен 2007-2022 годами. По данной теме выявлено 299 публикаций. Из них цели нашего исследования соответствовало 61 публикаций. *Критерии включения:* Публикации уровня доказательности А, В: мета-анализы, систематические обзоры, когортные и поперечные исследования. *Критерии исключения:* краткие отчеты, газетные статьи и личные сообщения.

Результаты и выводы. Папулопустулезная розацеа и демодекоз являются распространенными заболеваниями кожи лица, которые трудно диагностировать клинически. В дополнение к хорошо известным клиническим признакам, таким как сосудистые признаки и папулы, в нашем исследовании пациентов с известной папулопустулезной розацеа или демодекозом мы показали, что часто присутствуют и другие клинические признаки (незаметные фолликулярные чешуйки на лице, перхоть, фолликулит на коже головы, зуд лица или кожи головы). Следовательно, наличие этих признаков и симптомов должно побудить дерматологов провести дальнейшие диагностические тесты (например, недавно описанный тест, основанный на высокой плотности клещей демодекса, наблюдаемых в этих условиях), чтобы обеспечить точный диагноз.

Ключевые слова: *клещ демодекс, глазная поверхность,воспаление.*

Түйіндеме

АДАМ ДЕМОДЕКОЗЫ ПАТОЛОГИЯСЫНЫҢ ДАМУ ЕРЕКШЕЛІКТЕРІ. ӘДЕБИЕТТІК ШОЛУ

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Түйін. Демодекс - бұл адамдарда кездесетін ең көп таралған паразит, бірақ оның көз бетіне қатысты патогенділігі туралы аз мәлімет бар. Соңғы 20 жылдағы демодекске деген қызығушылықтың артуы осы кене және оның патогенетикалық рөлі туралы түсінігімізді кеңейтті. Әдебиеттегі демодекске деген қызығушылықтың артуына қарамастан, болашақ зерттеулерге көптеген кедергілер бар, сондықтан осы шолудың бөлімі анықтауға және әрі қарай қарастыруға арналған. Терминология, диагностикалық әдістер және демодексті емдеу тәсілдері тұрғысынан біркелкіліктің болмауы болашақ зерттеулерді салыстыруға кедергі болып қала береді. Бұл шолу демодекс туралы қазіргі заманғы білімді жинақтайды және адамдарда демодексті зерттеудің болашақ бағыттары үшін кейбір ұсыныстар ұсынады деп үміттенеді.

Іздеу стратегиясы. Зерттеу адам демодекозының патогенезінің дамуына арналған ағылшын және орыс тілдеріндегі толық мәтінді басылымдарды зерттеді. Әдебиеттерді іздеу барысында келесі іздеу жүйелері қолданылды: Pubmed, Web of science, Cyberleninka, Google Scholar кілт сөздер. Уақыт кезеңі 2007-2022 жылдармен белгіленді. Осы тақырып бойынша 299 жарияланым анықталды. Олардың ішінде біздің зерттеуіміздің мақсаты 61 басылымға сәйкес келді. *Қосу критерийлері:* А, В дәлелділік деңгейінің жарияланымдары: мета-талдаулар, жүйелі шолулар, когорттық және көлденең зерттеулер. *Шығару критерийлері:* қысқаша есептер, газет мақалалары және жеке хабарламалар.

Нәтижелер мен қорытындылар. Папулопустулярлы розацея және демодекоз-бұл клиникалық диагноз қою қиын бет терісінің жиі кездесетін аурулары. Тамырлы белгілер мен папула сияқты белгілі клиникалық белгілерден басқа, белгілі папулопустулярлы розацея немесе демодекозы бар пациенттерді зерттеуде біз басқа клиникалық белгілердің жиі кездесетінін көрсеттік (бетіндегі көрінбейтін фолликулалық таразылар, қайызғақ, бас терісіндегі фолликулит, бет немесе бас терісінің қышуы). Сондықтан, осы белгілердің болуы дәл диагнозды қамтамасыз ету үшін дерматологтарды қосымша диагностикалық сынақтарға итермелеуі керек (мысалы, осы жағдайларда байқалған демодекс кенелерінің жоғары тығыздығына негізделген жақында сипатталған тест).

Түйінді сөздер: *демодекс кенесі, көз беті, қабыну.*

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Introduction

Demodex, a genus of small parasitic mites infecting mammals, was first identified in 1841, but only recently attracted the attention of clinicians, including ophthalmologists, dermatologists and other specialists. Among the various types of mites, Demodex folliculorum and Demodex brevis are the only two that affect human skin. Because the eye is surrounded by protruding body parts such as the nose, eyebrow and cheek, it is not as accessible for daily hygiene as the rest of the body. Therefore, after infection with demodex occurs on the skin of the face, it is likely to spread and grow in the eye, which will lead to ocular demodecosis [34]. The morphology and habitats of the two demodex mites are different. The larger, D. folliculorum, about 0.3–0.4 mm long, is collected as a group in the hair follicle, while the smaller, D. brevis, about 0.2–0.3 mm long, is located separately in the sebaceous gland [8, 34]. Therefore, when sampling eyelashes, the probability of detecting D. folliculorum is much higher than the probability of detecting D. brevis in the general population and in patients with blepharitis [33]. The lifespan of demodex mites is about 3-4 weeks from the egg stage to the adult stage.Females can live another 5 days after oviposition [36].

The incidence of demodecosis infection increases with age, observed in 84% of the population aged 60 years and 100% of the population aged over 70 years. There are some risk factors that may predispose patients to the development of demodecosis of the eyes, such as rosacea, skin phototype, exposure to sunlight, alcohol consumption, smoking, stress, hot drinks, spicy food, sudden changes in temperature, and systemic immune status [28].

In the dermatology literature, demodex mites have been proposed as the causes of some skin diseases, such as follicular pityriasis, perioral dermatitis, rashes similar to scabies, facial pigmentation, rashes on bald scalp, demodicosis gravis and even basal cell carcinoma. In addition to skin diseases, ocular demodicosis is associated with a number of diseases of the external eyes, such as eyelash loss, improper alignment of eyelashes, blepharitis, conjunctivitis and blepharoconjunctivitis [15, 29–31, 34]. Interestingly, demodicosis was also associated with pterygium, meibomian gland dysfunction (MGD), vision-threatening keratitis, and basal cell carcinoma of the eyelid [19, 23].

Search strategy. The study examined full-text publications in English and Russian, which are devoted features of the pathology development of human demodicosis. In the process of searching for literature, the following search engines were used: Pubmed, Web of science, Cyberleninka, Google Scholar by keywords. The time period was designated 2007-2022. 299 publications were identified on this topic. Of these, 61 publications corresponded to the purpose of our study.

Results and discussion

Pathogenesis

The pathogenesis of demodex mites has been discussed for a long time [27]. This is partly due to the fact that demodecosis has a high prevalence depending on age and is often found on the skin of asymptomatic people. In the eye, a similar debate has been raised regarding blepharitis. It is assumed that demodex mites become pathogenic when they multiply and cause or worsen ocular symptoms and changes in the edge of the eyelid. However, none of the previous studies has convincingly demonstrated whether a minimum number of ticks should be present for symptoms to appear. Since humans are the sole host of demodex mites, no animal model of ocular demodecosis has been successfully created. A prospective cohort or controlled study on young patients in whom demodecosis infection is considered rare would confirm their pathogenic role in demodecosis. A possible causal relationship between demodex infection and eye inflammation can be further confirmed if the inflammation passes after tick-killing therapy [12].

The probable mechanism of action in case of demodex infection includes causing direct damage, acting as a bacterial carrier and inducing hypersensitivity. Firstly, demodex mites, especially D. folliculorum, absorb epithelial cells of the hair follicle, which leads to the expansion of the follicle. Microabrasions caused by tick claws additionally cause epithelial hyperplasia and reactive hyperkeratinization [3]. Meanwhile, D. brevis usually penetrates deep into the meibomian glands. In addition to mechanically blocking the openings of the meibomian glands, its chitinous exoskeleton can act as a foreign body and cause granulomatous reactions. Thus, demodex mites can be a potential cause of chalasia and MGD [15].Secondly, demodex mites carry associated bacteria such as streptococci and staphylococci on their surface, as well as Bacillus oleronius inside their abdomen [3, 30]. Thirdly, proteins inside ticks and their debris or waste can cause inflammatory reactions of the host through delayed hypersensitivity or innate immune responses [3].

Demodex and eye disease

Although demodex infection manifests itself with almost no symptoms, there are concomitant diseases that have been associated with its presence, such as blepharitis [54, 61], meibomian gland dysfunction (MGD) [32, 35], keratitis, blepharokeratoconjunctivitis [59], chalazion [33], dry eye [2], and pterygium [55]. The risk of demodex in patients with blepharitis is 2.5 times, while the risk in patients with rosacea is three times higher than in the general population [25]. Demodicosis can also contribute to general inflammation of the ocular surface, including blepharitis, MGD and keratitis. Elevated levels of cytokines, chemokines and other biomarkers of inflammation are significantly reduced after the start of therapy. Tear cytokines, in particular interleukin-17, which plays an important role in inflammation of the ocular surface and the edge of the eyelid, positively correlate with demodicosis [26]. Demodex mite has also been implemented as a potential carrier of bacteria transferred to its surface, transporting streptococci and staphylococci, which can cause further inflammatory reactions of surrounding tissues. In addition, since the male demodex has no anus, the digested material remains in the intestine and penetrates into the surrounding tissues at the end of its life cycle [43, 57]. Bacillus oleronius, a bacterium isolated from the gut of D. folliculorum, produces antigens capable of provoking an immune response [16, 25, 30, 44]. Demodicosis in skin lesions, especially the face, is well documented in dermatology [20, 50]. It is well established that a strong correlation exists between acne rosacea and Demodex,

whereby a seven- to eight-fold increased risk of having Demodex in acne rosacea patients exists [60]. As D. brevis resides in sebaceous glands, it can be found in many areas of the body including the face, particularly the cheek and nasal-labial folds10 as well as the meibomian glands of the eyelid, establishing a strong correlation between acne rosacea and MGD [45]. What was not evident, until recently, was the correlation between eyelash and facial demodicosis. A positive correlation between the severity of eyelash infestation by D. folliculorum and facial demodicosis was demonstrated in non-rosacea patients [1]. In addition, the presence of demodex has been shown to affect changes in the microstructure of the meibomian glands (acinar size, severity of fibrosis, reflectivity of the meibum, and more), especially in patients with MGD. As support for the coexistence of dermatological and ocular demodicosis grows, the possibility of joint patient management between ophthalmology and dermatology is likely to become more obvious. Other predisposing factors to demodicosis include immunodeficiency and those suffering from depression. It was also revealed that those who wear contact lenses have a higher number of demodex mites, and this may be a factor in intolerance to contact lenses and subsequent rejection of them. Clinicians should consider Demodex as part of their differential diagnosis when a contact lens user complains of discomfort. Other factors that can affect the immune system and, consequently, predisposition to demodicosis include emotional stress, poor nutrition, poor sleep, ultraviolet phototherapy, skin tumors and concomitant diseases [16].

Diagnosis

The diagnosis of demodicosis is mainly based on clinical evaluation and is confirmed by microscopic detection of demodex mites in epilated eyelashes. Thus, the clinical diagnosis is inaccurate. Symptoms such as blepharitis, blepharoconjunctivitis, rosacea of the eyes, eyelash diseases and chalasia may be suspected of infection with demodex. CD is a reliable diagnostic feature. When examined with a slit lamp, CD has the appearance of hardened exudative secretions around the base of the eyelashes.

Detection of demodex can be easily performed by ophthalmologists or technicians. In short, two eyelashes per CD per eyelid are removed with thin forceps under a slit lamp. Sampling eyelashes with CD is more likely to give good results than random hair removal [24]. Under a light microscope, one drop of saline solution is pipetted to the edge of the cover glass before examination. For those who still have a CD, adding one drop of a solution of fluorescein, peanut butter or 75% alcohol can help the built-in demodex migrate outwards. The biggest question is the maximum number of ticks detected. Since demodex mites can be found in asymptomatic populations, it remains unclear how many eyelashes should be selected and how many mites are capable of causing pathological changes.

Recently, confocal laser scanning microscopy in vivo (CLSM) was used to detect demodex infection [49]. Demodex ticks are presented in the form of rounded or long cone-shaped structures with CLSM. However, in most cases it is difficult to distinguish between the two types of demodex mites with CLSM. In addition, the patient's cooperation is extremely necessary.

Diagnosis of demodicosis in children is a difficult task, if not problematic, because of their poor interaction during epilation. CD in children is not as obvious as in adults. In addition, the number of demodexes in children is generally lower than in adult patients, presumably due to the relatively shorter period of infection. Therefore, to establish the diagnosis of demodecosis of the eyes, it may be justified to take a sample of a much larger number of eyelashes in children than is recommended in adults, especially when CD is not manifested. However, given that demodecosis is considered zero or very rare among the general pediatric population, the detection of any number of ticks is of great importance.

Treatment

Demodex mites are resistant to a wide range of antiseptic agents, including 75% alcohol, 10% povidone-iodine and erythromycin [15]. By microscopic observation in vitro for 150 minutes, Gao et al. found that D. folliculorum can be killed by TTO depending on the dose. TTO not only cleanses the CD from the roots of the eyelashes, but also stimulates the penetration of mites on the skin. In addition to destroying demodex, TTO has antibacterial, antifungal, and anti-inflammatory effects.

Patients with demodicosis of the eyes are recommended to use Cliradex®, which contains TTO as an active component, as an eye scrub twice a day for 3 months to destroy demodex mites. In particular, after washing the face and eyelids with baby shampoo or soap and rinsing with warm water, Cliradex® is applied to the roots of the eyelashes both along the upper and lower edge of the eyelid with closed eyes.

Thus, demodex mites are the most common microscopic ectoparasites found in human skin and eye. Demodex infection is often overlooked in clinical studies of inflammatory diseases of the ocular surface and may be the cause of the ineffectiveness of antibacterial and antiviral treatment. Although its pathogenesis has been discussed for a long time, more and more evidence suggests that demodex infection is a potential cause of inflammation of the ocular surface in blepharitis, blepharoconjunctivitis, MHD, pterygium, chalasia, basal cell carcinoma of the eyelid and keratitis, threatening vision.

Treatment of demodicosis is not aimed at eradication, but rather at reducing the number of ticks to restore the balance of the ecology of the ocular surface [14]. Thus, the role of demodex as a parasite-commensal is still recognized by some authors [9, 42]. A limited number of antiseptics have demonstrated the ability to destroy the tick in vitro, including tea tree oil (TTO) [22, 41], cumin and dill oil, sage and peppermint oil and pilocarpine gel. Much attention has been paid to TTO, as it attracts the demodex mite from the eyelash follicle in a dose-dependent way, keep in mind that 100% TTO is excessively irritating to the skin. TTO is obtained from the leaves of the Australian native tree Melaleuca alternifolia and contains known ingredients, of which the most common is terpinene-4-ol (T4O), which has a strong demodectic affinity [56]. An increasing number of eyelid hygiene products are available to combat infection with demodex [4, 58], containing either TTO or T4O in various concentrations [6, 38]. Linalool, alcohol, which is the main component of rosewood (Aniba rosaeodora) and camphor tree (Cinamomon camphora) oils., they have also

been found to have strong antimicrobial properties, including leishmanicidal effects. Eyelid hygiene products containing TTO, T4O, linalool or a combination thereof reduce the survival time of demodex, although the effectiveness of linalool alone requires further study [37]. Although most eyelid cleansers are well tolerated, it has been reported that some of them cause discomfort when applied, from a few seconds to a few minutes [40]. Trial testing of products in the office, combined with patient education, can help curb patient anxiety once at home [48]. Another problem in compliance with treatment recommendations occurs in those patients who do not have symptoms. Combination therapy also reduces the number of ticks. The combination of treatment in the office with 50% TTO with daily homemade eye scrubs TTO112 or eyelid wipes with microblefaroexfoliation in the office (the method of mechanical treatment and exfoliation of the edge of the eyelids) showed effectiveness in reducing the number of mites and eye symptoms. New substances to combat demodex include New Zealand Manuka honey (Leptospermum scoparium) containing methylglyoxal (MGO), free of peroxide, with increased resistance to enzymatic inactivation [7]. MGO Manuka Honey has shown comparable effects with 50% TTO in reducing the viability of demodex in vitro [13], and has good tolerability and safety profile as an eye cream formulation, but this has not yet been commercialized. Other emerging substances exhibiting antimicrobial properties include hypochlorous acid [51] and okra-based polysaccharide (Abelmoschus esculentus) [47]; however, their demodectic properties have yet to be demonstrated [21]. In most studies, the effectiveness of therapy is measured only on D. folliculorum, since ticks are more accessible than D. brevis. The effectiveness of therapy is measured as a reduction in the number of ticks or a reduction in survival time, measured as the absence of movement of the legs or mouth. As mentioned earlier, observing the decreasing autofluorescence of propidium iodide dye determines the point of death 11 with greater accuracy and may be more suitable for assessing demodectic activity. Oral medications have also been considered in refractory cases of ocular demodicosis. Oral ivermectin is a broad-spectrum antiparasitic agent that effectively reduces demodex infection [17, 52, 53]. Combination therapy with ivermectin and metronidazole proved to be more effective than ivermectin alone in reducing the number of D mites. infection with follicle and gives hope for future therapeutic options for refractory cases. Additional therapy and recommendations may include cleansing the face twice a day, avoiding oil-based cleansers and oily cosmetics, as well as regular exfoliation of the skin to remove dead cells [50]. One study of demodex on the face showed that the use of makeup appears to be protective, as it can prevent the formation of skin follicles and prevent the transmission of ticks. It is also assumed that those who use cosmetics, they can clean their face more often [18]. In case of any concomitant facial abnormalities, it is also recommended to consult a dermatologist. It has been suggested that excessive use of creams/moisturizers should be avoided, as this may be an additional lipid nutrition for demodex. The rejection of lipid-based eye drops during demodicosis infection has not been documented; however, it has been reported that the survival time of demodex increases with oil-based immersion, for example mineral oil, which is part of several artificial tears and ointments. Further research will be required to confirm this thesis. A recent meta-analysis evaluated the effectiveness of both local and systemic treatments for demodex blepharitis. Although all treatments reduced the number of ticks and reduced symptoms, stratified meta-analysis did not reveal any significant difference between local and systemic treatments [39]. Given the potential side effects of systemic medications, it may be recommended to start treatment with local therapy and reserve systemic options for more complex cases. Intense Pulsed light (IPL) is used for various medical and aesthetic skin diseases [46]. He has shown promising results in the treatment of demodicosis [5, 10], including in patients with rosacea and with eye damage. In one study, during which IPL was performed three times (initially, after 30 and 90 days), the level of elimination of demodex was 55% with IPL for one month and a significant improvement in lacrimation. time, evaluation of the quality of meibum and the Ocular Surface Diseases Index (OSDI) after three months in favor of IPL. At present, the exact mechanism explaining the effect of IPL on Demodex has not yet been fully elucidated; However, it has been suggested that demodex mites may be sensitive to the energy supplied during the IPL and/or the heat generated, which may raise the temperature to critical levels for their destruction. Real-time video recording in vitro IPL showed that the temperature of the microscope slide reaches 49°C with complete immobilization of the tick (retraction and lack of leg movement) within 25 seconds after IPL [11]. This phenomenon requires further clinical investigation.

Conclusion.

Papulopustular rosacea and demodecosis are common facial skin diseases that can be difficult to diagnose clinically. In addition to well-known clinical signs such as vascular signs and papules, in our study of patients with known papulopustular rosacea or demodecosis, we have shown that other clinical signs are also often present (inconspicuous follicular scales on the face, dandruff, folliculitis on the scalp, itching of the face or scalp). Therefore, the presence of these signs and symptoms should encourage dermatologists to conduct further diagnostic tests (for example, the recently described test based on the high density of demodex mites observed in these conditions) to ensure an accurate diagnosis.

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References:

1. *Aumond S., Bitton E.* Palpebral and facial skin infestation by Demodex folliculorum // Contact lens & anterior eye : the journal of the British Contact Lens Association. 2020. № 2 (43). С. 115–122.

2. *Ayyildiz T., Sezgin F.M.* The Effect of Ocular Demodex Colonization on Schirmer test and OSDI Scores in Newly Diagnosed Dry Eye Patients // Eye & contact lens. 2020. (46 Suppl 1). C. S39–S41.

3. *Bevins C.L., Liu F.T.* Rosacea: skin innate immunity gone awry? // Nature medicine. 2007. № 8 (13). C. 904–906.

4. *Bitton E., Ngo W., Dupont P.* Eyelid hygiene products: A scoping review // Contact lens & anterior eye : the journal of the British Contact Lens Association. 2019. № 6 (42). C. 591–597.

5. *Cheng S. et al.* Intense Pulsed Light Therapy for Patients with Meibomian Gland Dysfunction and Ocular Demodex Infestation // Current medical science. 2019. № 5 (39). C. 800–809.

6. *Cheung I. et al.* In vitro anti-demodectic effects and terpinen-4-ol content of commercial eyelid cleansers // Contact lens & anterior eye : the journal of the British Contact Lens Association. 2018. № 6 (41). C. 513–517.

7. *Craig J.P. et al.* Preclinical development of MGO Manuka Honey microemulsion for blepharitis management // BMJ open ophthalmology. 2017. № 1 (1), P.1-12.

8. *Elston C.A., Elston D.M.* Demodex mites // Clinics in Dermatology. 2014. № 6 (32). C. 739–743.

9. E*lston D.M.* Demodex mites: facts and controversies // Clinics in dermatology. 2010. № 5 (28). C. 502–504.

10. E*rtaş R. et al..* The rapid effect of pulsed dye laser on demodex density of facial skin // Journal of cosmetic and laser therapy : official publication of the European Society for Laser Dermatology. 2019. № 3 (21). C. 123–126.

11. *Fishman H.A., Periman L.M., Shah A.A.* Real-Time Video Microscopy of In Vitro Demodex Death by Intense Pulsed Light // Photobiomodulation, photomedicine, and laser surgery. 2020. № 8 (38). C. 472–476.

12. *Foley R. et al.* Demodex: a skin resident in man and his best friend // Journal of the European Academy of Dermatology and Venereology : JEADV. 2021. № 1 (35). C. 62–72.

13. *Frame K. et al.* Comparing the in vitro effects of MGO ™ Manuka honey and tea tree oil on ocular Demodex viability // Contact lens & anterior eye : the journal of the British Contact Lens Association. 2018. № 6 (41). C. 527–530.

14. *Fromstein S.R. et al.* Demodex blepharitis: clinical perspectives // Clinical optometry. 2018. (10). C. 57–63.

15. *Gao Y.Y. et al.* Clinical treatment of ocular demodecosis by lid scrub with tea tree oil // Cornea. 2007. № 2 (26). C. 136–143.

16. *Gazi U., Taylan-Ozkan A., Mumcuoglu K.Y.* Immune mechanisms in human and canine demodicosis: A review // Parasite immunology. 2019. № 12 (41), P.1-7.

17. *Holzchuh F.G. et al.* Clinical treatment of ocular Demodex folliculorum by systemic ivermectin // American journal of ophthalmology. 2011. № 6 (151), P.1030-1034.

18. *Horváth A. et al.* Risk factors and prevalence of Demodex mites in young adults // Acta microbiologica et immunologica Hungarica. 2011. № 2 (58). C. 145–155.

19. *Huang Y. et al.* Ocular demodicosis as a risk factor of pterygium recurrence // Ophthalmology. 2013. № 7 (120). C. 1341–1347.

20. J*armuda S. et al.* Potential role of Demodex mites and bacteria in the induction of rosacea // Journal of medical microbiology. 2012. № Pt 11 (61). C. 1504–1510.

21. *Kabat A.G.* In vitro demodicidal activity of commercial lid hygiene products // Clinical ophthalmology (Auckland, N.Z.). 2019. (13). C. 1493–1497.

22. *Karakurt Y., Zeytun E.* Evaluation of the Efficacy of Tea Tree Oil On the Density of Demodex Mites (Acari: Demodicidae) and Ocular Symptoms In Patients With Demodectic Blepharitis // The Journal of parasitology. 2018. № 5 (104). C. 473–478.

23. *Kheirkhah A. et al.* Corneal manifestations of ocular demodex infestation // American journal of ophthalmology. 2007. № 5 (143),P.743-749.

24. *Kheirkhah A. et al.* Fluorescein dye improves microscopic evaluation and counting of demodex in blepharitis with cylindrical dandruff // Cornea. 2007. № 6 (26). C. 697–700.

25. *Kim J.H., Chun Y.S., Kim J.C.* Clinical and immunological responses in ocular demodecosis // Journal of Korean medical science. 2011. № 9 (26). C. 1231–1237.

26. *Kim J.T. et al.* Tear cytokines and chemokines in patients with Demodex blepharitis // Cytokine. 2011. № 1 (53). C. 94–99.

27. *Kligman A.M., Christensen M.S.* Demodex folliculorum: requirements for understanding its role in human skin disease // The Journal of investigative dermatology. 2011. № 1 (131). C. 8–10.

28. *Kulac M. et al.* Clinical importance of Demodex folliculorum in patients receiving phototherapy // International journal of dermatology. 2008. № 1 (47). C. 72–77.

29. *Lee S.H. et al.* The relationship between demodex and ocular discomfort // Investigative ophthalmology & visual science. 2010. № 6 (51). C. 2906–2911.

30. *Li J. et al.* Correlation between ocular Demodex infestation and serum immunoreactivity to Bacillus proteins in patients with Facial rosacea // Ophthalmology. 2010. № 5 (117).

31. *Liang L. et al.* Ocular demodicosis as a potential cause of pediatric blepharoconjunctivitis // Cornea. 2010. № 12 (29). C. 1386–1391.

32. *Liang L. et al.* Significant correlation between meibomian gland dysfunction and keratitis in young patients with Demodex brevis infestation // The British journal of ophthalmology. 2018. № 8 (102). C. 1098–1102.

33. *Liang L., Ding X., Tseng S.C.G.* High prevalence of demodex brevis infestation in chalazia // American journal of ophthalmology. 2014. № 2 (157), P.1-20.

34. *Liu J., Sheha H., Tseng S.C.G.* Pathogenic role of Demodex mites in blepharitis // Current opinion in allergy and clinical immunology. 2010. № 5 (10). C. 505–510.

35. *López-Ponce D. et al.* High prevalence of Demodex spp. infestation among patients with posterior blepharitis: correlation with age and cylindrical dandruff // Archivos de la Sociedad Espanola de Oftalmologia. 2017. № 9 (92). C. 412–418.

36. *Luo X. et al.* Ocular Demodicosis as a Potential Cause of Ocular Surface Inflammation // Cornea. 2017. № Suppl 1 (36 Suppl 1). C. S9–S14.

37. *Messaoud R. et al.* Improvement in ocular symptoms and signs in patients with Demodex anterior blepharitis using a novel terpinen-4-ol (2.5%) and hyaluronic acid (0.2%) cleansing wipe // Clinical

ophthalmology (Auckland, N.Z.). 2019. (13). C. 1043–1054.

38. M*urphy O., O'Dwyer V., Lloyd-McKernan A.* The efficacy of tea tree face wash, 1, 2-Octanediol and microblepharoexfoliation in treating Demodex folliculorum blepharitis // Contact lens & anterior eye : the journal of the British Contact Lens Association. 2018. № 1 (41). C. 77–82.

39. *Navel V. et al.* Efficacy of treatments for Demodex blepharitis: A systematic review and meta-analysis // The ocular surface. 2019. № 4 (17). C. 655–669.

40. *Ngo W., Jones L., Bitton E.* Short-Term Comfort Responses Associated With the Use of Eyelid Cleansing Products to Manage Demodex folliculorum // Eye & contact lens. 2018. (44 Suppl 2). C. S87–S92.

41. N*icholls S.G. et al.* Demodex treatment in external ocular disease: the outcomes of a Tasmanian case series // International ophthalmology. 2016. № 5 (36). C. 691–696.

42. *Nicholls S.G. et al.* Demodex species in human ocular disease: new clinicopathological aspects // International ophthalmology. 2017. № 1 (37). C. 303–312.

43. *O'Reilly N. et al.* Demodex-associated bacterial proteins induce neutrophil activation // The British journal of dermatology. 2012. № 4 (166). C. 753–760.

44. *O'Reilly N., Menezes N., Kavanagh K.* Positive correlation between serum immunoreactivity to Demodex-associated Bacillus proteins and erythematotelangiectatic rosacea // The British journal of dermatology. 2012. № 5 (167). C. 1032–1036.

45. *Palamar M. et al.* Evaluation of dry eye and meibomian gland dysfunction with meibography in patients with rosacea // Cornea. 2015. № 5 (34). C. 497–499.

46. *Papageorgiou P. et al.* Treatment of rosacea with intense pulsed light: significant improvement and long-lasting results // The British journal of dermatology. 2008. № 3 (159). C. 628–632.

47. *Petropoulos S. et al.* The chemical composition, nutritional value and antimicrobial properties of Abelmoschus esculentus seeds // Food & function. 2017. № 12 (8). C. 4733–4743.

48. *Qiu T.Y., Yeo S., Tong L.* Satisfaction and convenience of using terpenoid-impregnated eyelid wipes and teaching method in people without blepharitis // Clinical ophthalmology (Auckland, N.Z.). 2018. (12). C. 91–98.

49. *Randon M. et al.* In vivo confocal microscopy as a novel and reliable tool for the diagnosis of Demodex eyelid infestation // The British journal of ophthalmology. 2015. № 3 (99). C. 336–341.

50. R*ather P.A., Hassan I.* Human demodex mite: the versatile mite of dermatological importance // Indian journal of dermatology. 2014. № 1 (59). C. 60–66.

51. R*omanowski E.G. et al.* In Vitro Evaluation of a Hypochlorous Acid Hygiene Solution on Established Biofilms // Eye & contact lens. 2018. № Suppl 2 (44 Suppl 2). C. S187–S191.

52. *Salem D.A.B. et al.* Evaluation of the efficacy of oral ivermectin in comparison with ivermectin-metronidazole combined therapy in the treatment of ocular and skin lesions of Demodex folliculorum // International journal of infectious diseases : IJID : official publication of the International Society for Infectious Diseases. 2013. № 5 (17).P.342-347.

53. *Schaller M., Pietschke K.* Successful therapy of ocular rosacea with topical ivermectin // The British journal of dermatology. 2018. № 2 (179). C. 520–521.

54. *Sedzikowska A., Oseka M., Skopinski P.* The impact of age, sex, blepharitis, rosacea and rheumatoid arthritis on Demodex mite infection // Archives of medical science : AMS. 2018. № 2 (14). C. 353–356.

55. *Tarkowski W., Moneta-Wielgoś J., Młocicki D.* Do Demodex mites play a role in pterygium development? // Medical hypotheses. 2017. (98). C. 6–10.

56. *Tighe S., Gao Y.-Y., Tseng S.C.G.* Terpinen-4-ol is the Most Active Ingredient of Tea Tree Oil to Kill Demodex Mites // Translational vision science & technology. 2013. № 7 (2). C. 2.

57. *Wesolowska M. et al.* Prevalence of Demodex spp. in eyelash follicles in different populations // Archives of medical science : AMS. 2014. № 2 (10). C. 319–324.

58. *Wong K. et al.* The effect of Blephadex™ Eyelid Wipes on Demodex mites, ocular microbiota, bacterial lipase and comfort: a pilot study // Contact lens & anterior eye : the journal of the British Contact Lens Association. 2019. № 6 (42). C. 652–657.

59. *Wu M. et al.* Evaluation of the ocular surface characteristics and Demodex infestation in paediatric and adult blepharokeratoconjunctivitis // BMC ophthalmology. 2019. № 1 (19),P.2-7.

60. *Zhao Y.E. et al.* Retrospective analysis of the association between Demodex infestation and rosacea // Archives of dermatology. 2010. № 8 (146). C. 896–902.

61. *Zhao Y.E. et al.* Association of blepharitis with Demodex: a meta-analysis // Ophthalmic epidemiology. 2012. № 2 (19). C. 95–102.

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