JOURNAL OF BIOLOGICAL RESEARCH AND REVIEWS
2024; 1(1): 21-26.
10.5455/JBRR.20240222074805

RESEARCH ARTICLE

Open Access

Estimation of a mucosal cytokine concentration associated with a bacterial eye infection

Anmar Mahdi Kadhim AL-Maamori, Shaimaa Jassim AlSultany
College of Science, University of Babylon, Hillah, Iraq

ABSTRACT

Aim and Background: Although eye infections are rather frequent, they pose a serious risk to one's eyesight and should be treated immediately. Bacteria in the air can contaminate the entire eye. However, T cells also contribute to the production of interleukin18 (IL-18), another pro-inflammatory cytokine that is also part of the IL-1 superfamily is mostly made by macrophages, and has pleiotropic effects, meaning it can affect and activate several cell types. The protein, known as tumor necrosis factor alpha (TNFα), is involved in cell signaling. While activated macrophages are the primary cells responsible for its production, several other cell types, including T cells (helper cells), Natural killer cells, neutrophils, mast cells, and eosinophils, are capable of doing so as well. The study aims to see the role of interleukin in eye infections.

Methods: From September 2020 through March 2021, 89 tear eye swabs were collected from patients with bacterial eye infections who were treated at the Al-Imam Al-Sadiq Hospital in Babylon, the Ibn Al-Haitham Teaching Eye Hospital in Baghdad, and the Specialized Ophthalmology clinics in Babylon were collection from healthy persons as control samples.

Results: Immunological parameters IL-18 and (TNFα) were determined in tear by enzyme-linked immunosorbent assay The mean of IL-18 concentration in the tear of the patient was 148.10 ± 5.91 pg/ml, while the control was 108.34 ± 14.52*pg/ml there significantly. The mean of TNF-α concentration in the tear of the patient was 766.28 ± 37.84 pg/ml, while the control was 530.47 ± 89.99*pg/ml there significantly. The study has shown elevated points of inflammatory cytokines such as IL18 and TNFα in the tear film of patients.

ARTICLE HISTORY

Received February 22, 2024
Accepted April 06, 2024
Published April 13, 2024

KEYWORDS

Eye; IL-18 mucosal concentration; (TNF)-α; tear film.

Introduction

The ability to see is a vital sense for humans. Because dust, extreme heat, bacteria, and other agents can cause numerous eye disorders that can lead to blindness, it is crucial to promote healthy habits for maintaining clean living environments [1,2]. Infections such as bacteria, viruses, and fungi can affect the human eye, just as they can affect any other part of the body. Infectious bacteria in the eye is a serious medical issue that needs to be addressed [3,4]. Bacteria can spread from person to person by casual touch or through the air. Blepharitis, conjunctivitis, keratitis, and lacrimal sac infections are all documented forms of ocular illness [5,6]. Because of their virulence factor and the host's lowered resistance owing to factors including poor cleanliness, poor living conditions, poor diet, heredity, physiology, fever, and age, pathogenic microorganisms cause illnesses of the eyes [7–9]. Staphylococci are the most common Gram-positive eye isolates, whereas *Pseudomonas aeruginosa, Klebsiella pneumonia*, and *Escherichia coli* are the most common bacterial ocular pathogens [10,11].

Tear film

In the fight against microbes, this acts as the front line of defense. Protection and lubrication of the eye's surface are two of tears' primary roles. The

Contact Shaimaa Jassim AlSultany shamajasm99@gmail.com College of Science, University of Babylon, Hillah, Ira.

lacrimal functional unit is responsible for controlling tear production, distribution, and clearance; tears play an important role in preserving healthy eye function by, e.g., warding off dryness and protecting the eye from environmental irritants and infection-causing microorganisms. Tears wipe away any foreign bodies in the eye [12,13]. Lysozyme, Lipocalin, Lactoferrin, and mucin are all found in tears [14]. Dendritic cells (DCs) in conjunctivitis inflammation release cytokines such as interleukin (IL-6) and gamma interferon, which increase goblet cell mucin synthesis and secretion [15].

Immunity of ocular

The immunology of the ocular surface is a remarkable example of the relationship concerning the native and adaptive immune systems since it consists of a complex array of defense mechanisms that work to prevent microbial colonization [16]. Ocular immunity relies heavily on the innate immune system, which acts as the primary host route of resistance alongside imported invaders. Epithelium on the surface of the eye can generate inflammatory cytokines such as interleukin ocular surface epithelium contains interleukin-1 beta (IL-1 beta), tumor necrosis factor-alpha (TNFα), interleukin-6, interleukin-8, and all isoforms of human beta-defenses [17]. Goblet cells, DCs, macrophages (innate), T cells, B cells, and others reside in the ordinary conjunctiva epithelium and sub-epithelial stroma (adaptive) [18].

The role of interleukin18 (IL-18) and TNF- α in bacterial eye infection

IL18 is a proinflammatory cytokine that has a function in both acquired immunity and innate immunity. It is an associate of the IL-1 family of cytokines, which is a family of cytokines. It is primarily created by macrophages, monocytes, and DCs in reaction to stimuli of viral or bacterial origin. One of the results of innate immunity, which is begun by host-pathogen contact, is the synthesis of IL-18 [19], and this is one of the effects. There is a connection between IL-18 and infections produced by bacteria and viruses [20]. In the presence of IL-12, one of the most important roles that IL-18 plays is to encourage the creation of the cytokine known as interferon gamma (IFN-) by T and natural killer (NK) cells. Following infection with a number of different microbial products, such as lipopolysaccharide, and exotoxins from Gram-positive bacteria, it stimulates cell-mediated immunity together with IL-12 [21]. The three members of the IL-1 private that are most commonly associated with retinal degenerative disorders are IL-1, IL-18, and IL-1 [22].

TNF is a proinflammatory cytokine that is mainly created by triggered macrophages, T lymphocytes, and NK cells, in addition to other cells such as B-cells, neutrophils, and endothelial cells. This tiny protein is used by the immune system for cell communication [23]. TNF-a plays a dual role in the body, first as a pro-inflammatory mediator, which causes a heavy-duty inflammatory reply, and then as an immunosuppressive mediator, which limits the point and extent of inflammatory developments and inhibits the enlargement of autoimmune diseases, tumor genesis, and epithelial apoptosis TNF-a is responsible for initiating a strong inflammatory response when it acts as a pro-inflammatory mediator [20].

The aim of this research refers to measuring the concentration of human IL-18 and TNF- in patients' tear films and serums using enzyme-linked immunosorbent assay (ELISA).

Materials and Methods

Specimen's collection

Eighty-nine eye swabs were collected from patients who were suffering from a bacterial eye infection who attended Al-Imam Al-Sadiq Hospital/Babylon, and Ibn Al-Haitham Teaching Eye Hospital/ Baghdad, from September 2020 to March 2021, and 20 swabs were collected from healthy persons as control specimens, by using sterile swabs included one swab (for bacterial diagnosis of the affected part of the eye), and other swab tears from secreted tears (for some immunological parameters detection) for both sexes. IL-18 and TNFα cytokines were valued in the patient and controlled by using an ELISA depending on the principle of the manufactured company (Elabscience, china).

Statistical analysis

SPSS was carried out for the data analysis (version 20, SPSS Inc. Chicago, IL). A *T*-test was used to associate evocative data (mean, standard error) and alterations at the p 0.05 level.

Results and Discussions

This study investigated the values of IL-18 and TNFα in the tear of the bacterial eye infection patient and compared them with those non-infection people. The study has shown elevated levels of

inflammatory cytokines such as IL-18 and TNFα in the tear film of patients.

The mean of IL-18 concentration in the tear of patients was 148.10 ± 5.91 pg/ml, while control was 108.34 ± 14.52*pg/ml there significantly. The mean of TNF-α concentration in the tear of the patient was 766.28 ± 37.84 pg/ml while the control was 530.47 ± 89.99*pg/ml there significantly shown in the Table 1.

In addition to monocytes and macrophages, other cell types that can produce IL 18 include DCs, epithelial cells, chondrocytes, osteoblasts, Kupffer cells, keratinocytes, astrocytes, and renal tubular epithelial cells. IL 18 is a pro-inflammatory member of the IL-1 family of cytokines that facilitates a type 1 response. When it comes to protecting the body from pathogens such as bacteria, fungus, and protozoa that live inside cells, IL 18 is the endogenous hero [20,21,24]. IL-18 plays a crucial role in the host's immune response against a wide variety of pathogenic microorganisms by greatly increasing the synthesis of IFN-, nitric oxide, and reactive oxygen species in phagocytes. IL-18's ability to induce IFN- in the nucleus is the single most important biological characteristic that sets it apart from IL-1. IL-12 is present. This capability is absent in IL-1. Furthermore, IL-18 directly activates CD8+ T cells, which play a crucial role in the process of eradicating viruses. In addition, IL-18 functions defensively in helminth infection because it increases Th2 cytokine production and granulocytes in the absence of IL-12 [25]. TNF- is one of many pro-inflammatory cytokines important for the start and maintenance of inflammation during autoimmune reactions, and it is produced by a wide diversity of cell kinds with macrophages, NK cells, CD4+ lymphocytes, adipocytes, T-cells, fibroblasts, astrocytes, and others. TNF- influences inflammatory responses, apoptosis, cytokine production, cell proliferation, and anti-infection efforts [26–28].

Several types of cytokines are current in tears to keep the situation of the ocular exterior and 25 cytokines and chemokines were noticed in tears from strong matters [29,30].

The tear concentration of IL-18 and TNF- α was significantly increased in tears of patients with bacterial eye infection at *p*-value <0.05 when compared to controls, as shown in Table 1. The results showed that TNF-α was the predominant interleukin in bacterial eye infection cases followed by IL-18, the mean levels of TNF-α (766.28 ± 37.84) and IL-18 was (148.10 ± 5.91) in tear specimens using an ELISA assay.

Table 1. Concentration of IL-18 and TNF-α patients and control in mucosal.

Groups \ Parameters	IL-18	TNF- α
	Mean ± S.E	
Patients	148.10 ± 5.91	766.28 ± 37.84
Control	108.34 ± 14.52*	530.47 ± 89.99*
p-value	0.044	0.037

*means a major alteration in contrast with control at the 0.05 level.

In this study, the tear concentrations of IL-18 were elevated in the affected eyes compared with the control, this might agree with the study obtained by Yamaguchi et al. [31]. They reported that the tear concentrations of IL-1β, IL-6, and IL-8 were elevated in the affected eyes with bacterial keratitis (BK). In addition, IL-1 beta and interleukin-18 assist the host's defense against infection by enhancing the antibacterial capabilities of phagocytes and beginning the adaptive immune responses of Th1 and Th17. Inflammasomes are protein complexes that catalase the autocatalytic activation of intracellular caspase-1, which in turn cleaves the inactive precursors of cytokines IL-1 and IL-18 into their mature, functional forms [31,32].

Researchers Mahajan et al. [33] found that patients with meibomian gland dysfunction have higher levels of neutrophil chemoattractants in their tear fluid (C5a, IL-6, IL-8, and IL-18). There was a correlation between increased amounts of C5a and IL-8 and decreased levels of tear fluid production. In comparison to healthy controls, individuals with an ocular bacterial infection had a significantly higher concentration of TNF- in their tear fluids. This was one of the findings of the current analysis. This is in line with the findings of Kopp and Ghosh [34] and Xue et al. [35], who discovered that the production of TNFα was increased during corneal inflammation. This indicates that the management of TNF may be chief in the treatment of corneal inflammation. The manufacture of cytokines results in the inflammation that occurs in the eye. The overexpression of pro-inflammatory cytokines such as TNF-, which cause irritation and a robust immune reaction, consequently contributing to corneal damage, was found to have a correlation with nuclear factor- B protein, which is one of the primary transcription factors. adding to this, according to AL-Rubaey et al. [36], it was observed

that there was a noticeable rise in the release of IL-6, IL-8, and TNF- in active epidemic keratoconjunctivitis (EKC) cases after being matched to controls tears, and the concentrations of IL-6, IL-8, and TNF- were considerably larger in tears of patients with EKC when compared to controls at *p*-values.

Konstantopoulos et al. [37] studied the levels of the group of cytokines and chemokines for BK patients such as IL-2, IL-8, IL-12p70, IL-1β, GM8, CSF, IFN-γ, IL-6, IL-10, and TNF-α and they observed that all cytokines/chemokine were elevated in tear specimens of BK patients except for IL-12p70. The highest attention percentages of (BK) to controls stayed practical for IL-1β, IFN-γ, IL-10, IL-6, and IL-8. Tears might be an applicable cause of biomarker because of the frequency of the inflammatory process. Furthermore, the collection of tears is easy and non-invasive [38].

Table 2 compares each patient cohort to a matched control cohort. The data suggested that in all age categories except the second group (ages 26–45), mucosal concentrations of IL-18 in controls were higher than in patients. Except for the second group, which showed the reverse trend, TNF- (mucosal) concentrations were higher in the control groups.

Since the ocular surface is not just a portion of the optical efficient part but also an immunological part per the capacity to reply to exterior inducements, the results for the IL-18 and TNF- in the mucosal levels indicate that the ocular mucosal immune system protects the eye against allergic, inflammatory, and infectious disease. Besides acting as a somatic wall sandwiched between the eye and external and internal stimuli, the tear film similarly holds soluble mucins and a number of immunoregulatory factors, including IFN-, as well as proinflammatory cytokines IL-1, TNF-, and is free from the anxious ocular superficial epithelium, which endorses the maturation of antigen-presenting cells (APCs).

Table 2. Concentration of IL-18 and TNF-α of the patients and control in mucosal according to age group.

Age/years	Cytokine pg./ml Mean ± S.E	
	IL-18 mucosal	TNF-α mucosal
5–25 years	130.72 ± 24.84	786.93 ± 33.45
Control	176.89 ± 21.54	985.59 ± 50.12
p- value	0.061	0.040*
26–46 years	154.11 ± 32.51	752.38 ± 18.91
Control	134.93 ± 34.22	680.09 ± 24.61
p- value	0.051	0.034*
46–65 years	160.95 ± 39.14	777.80 ± 98.65
Control	222.51 ± 33.41	1,018 ± 140.21
p- value	0.021*	0.005*

*mean significant difference in comparison with the control at the 0.05 level.

There are many bacteria associated with eye infection [39]. Modules of the innate immune system that sense pathogen mechanisms are current in ocular cells, and initiation consequences in the creation of proinflammatory cytokines, and APCs which comprise dendritic, B, and T cells. Ramos et al. [40] said that the eye has been regarded as an immune-privileged site that mechanisms of the innate immune system that sense pathogen mechanisms are current in ocular cells. Langerhans cells, which are important for awarding antigens to the adaptive immune system, are current in the epithelium of the cornea, iris, and retina. These cells have the ability to impasse and develop antigens, after that, they can traffic to the local draining lymph node or the spleen, which results in antibody production.

Correlation between IL-18 and TNF-α in bacterial eye patients

There was a negative connection between IL-18 mucosal and TNF-mucosal, while the *p*-value did not extend statistical significance at p 0.05. As can be seen in Figure 1, the researchers Engelbrecht et al. [41] could not discover any statistically significant differences in the quantities of cytokines discovered in the tears, including IL-1, IL-1, IL-2, IL-3, IL-4, IL-5, IL-7, IL-8, TNF, TNF, and VEGF. Ocular diseases of various types, particular biomarkers that can be found in tears have been related to a variety of diseases, either primary or secondary to systemic conditions. A recent study conducted by Zheng et al. [42] discovered that elevated amounts of VGEF, IL-12, IFN-, IL-10, CXCL9, and CCL3 were present in the aqueous humor of patients who had cataracts. This finding was observed to correlate with the patients' ages. Also components of cell wall lipopolysaccharide of some bacteria play role in immunity [43].

Conclusion

The interleukin family is a major subset of the cytokine superfamily, which consists of tiny produced proteins that fix to exact membrane receptors on goal cells. To fight against bacterial ocular infection, patients must produce more cytokines (IL-18 and TNF-α) in their tears.

References

1. Nabat ZN, Al-Kazazz ZK, Mokif TA. Isolation and identification of bacteria from patients with eye infection and study of some inflammatory cytokines in patients. Indian J Forensic Med Toxicol 2019; 13(4):813–7.
2. Summaiya A, Neeta K, Sangita R. Ocular infections: rational approach to antibiotic therapy. Nat J Med Res 2012; 2(1):22–4.
3. Shiferaw B, Gelaw B, Assefa A, Assefa Y, Addis Z. Bacterial isolates and their antimicrobial susceptibility pattern among patients with external ocular infections at Borumeda hospital, Northeast Ethiopia. BMC Ophthalmol 2015; 15:103.
4. Alfonso SA, Fawley JD, Alexa Lu X. Conjunctivitis. Prim Care 2015; 42(3):325–45.
5. Getahun E, Gelaw B, Assefa A, Assefa Y, Amsalu A. Bacterial pathogens associated with external ocular infections alongside eminent proportion of multidrug resistant isolates at the University of Gondar Hospital, northwest Ethiopia. BMC Ophthalmol 2017; 17(151):2–10.
6. Smith AF, Waycaster C. Estimate of the direct and indirect annual cost of bacterial conjunctivitis in the United States. BMC Ophthalmol 2009; 9(13):1–13.
7. Beceiro A, Tomás M, Bou G. Antimicrobial resistance and virulence: a successful or deleterious association in the bacterial world?. Clin Microbiol Rev 2013; 26(2):185–230.
8. Abid AJ, Ewadh RM. Etiology of bacterial eye infections and determination of immune response of infected patient. Medl J Babylon 2012; 9(4):799–805.
9. Watson S, Aguas MC, Khoo P. Common eye infections. Aust Prescr 2018; 41(3):67–72.
10. Teweldemedhin M, Saravanan M, Gebreyesus A, Gebreegziabiher D. Ocular bacterial infections at Quiha Ophthalmic Hospital, Northern Ethiopia: an evaluation according to the risk factors and the antimicrobial susceptibility of bacterial isolates. BMC Infect Dis 2017; 17(207):2–11.
11. Thomas RK, Melton R, Asbell PA. Antibiotic resistance among ocular pathogens: current trends from the ARMOR surveillance study (2009–2016). Clin Optom (Auckl) 2019; 11:15–26.
12. Kalló G, Emri M, Varga Z, Ujhelyi B, Tőzsér J, Csutak A, et al. Changes in the chemical barrier composition of tears in Alzheimer's disease reveal potential tear diagnostic biomarkers. J PLoS One 2016; 11(6):e0158000.
13. Pflugfelder SC, Stern ME. Biological functions of tear film. Exp Eye Res 2020; 197:108115.
14. Hori Y. Secreted mucins on the ocular surface. Invest Ophthalmol Vis Sci 2018; 59(14):DES151–6.
15. Gilger BC. Immunology of the ocular surface. Vet Clin Small Anim 2008; 38:223–31.
16. Song J, Huang YF, Zhang WJ, Chen XF, Guo YM. Ocular diseases: immunological and molecular mechanisms. Int J Ophthalmol 2016; 9(5):780–8.
17. Ueta M. Innate immunity of the ocular surface and ocular surface inflammatory disorders. Cornea 2008; 27(8):S31–40.
18. Kojima K, Ueta M, Hamuro J, Hozono Y, Kawasaki S, Yokoi N, et al. Human conjunctival epithelial cells express functional Toll-like receptor 5. Br J Ophthalmol 2008; 92:411–6.
19. Boraschi D, Dinarello CA. IL-18 in autoimmunity: review. Eur Cytokine Netw 2006; 17(4):224–52.
20. Akdis M, Aab A, Altunbulakli C, Azkur K, Costa RA, Crameri R, et al. Interleukins (from IL-1 to IL-38), interferons, transforming growth factor b, and TNF-a: receptors, functions, and roles in diseases. J Allergy Clin Immunol 2016; 138(4):984–1010.
21. Yasuda K, Nakanishi K, Tsutsui H. Interleukin-18 in health and disease. Int J Mol Sci 2019; 20(3):649.
22. Wooff Y, Man SM, Bruce RA, Natoli R, Fernando N. IL-1 family members mediate cell death, inflammation and angiogenesis in retinal degenerative diseases. Front Immunol 2019; 10:1618.
23. Zelová H, Hošek J. TNF-α signalling and inflammation: interactions between old acquaintances. Inflamm Res 2013; 62:641–51.
24. Tsutsui H, Nakanishi K. Immunotherapeutic applications of IL-18. Immunotherapy 2012; 4(12):1883–94; doi:10.2217/imt.12.137
25. Shen J, Choy DF, Yoshida T, Iwase T, Hafiz G, Xie B, et al. Interleukin-18 has antipermeablity and antiangiogenic activities in the eye; reciprocal suppression with VEGF. J Cell Physiol 2014; 229(8):974–83.
26. Valentincic NV, Groot-Mijnes JDF, Kraut A, Korosec P, Hawlina M, Rothova A. Intraocular and serum cytokine profiles in patients with intermediate uveitis. Mol Vis 2011; 17:2003–10.
27. Chen L, Deng H, Cui H, Fang J, Zuo Z, Deng J, et al. Inflammatory responses and inflammation-associated diseases in organs. Oncotarget 2018; 9(6):7204–18.
28. Mirshahi A, Hoehn R, Lorenz K, Kramann C, Baatz H. Anti-tumor necrosis factor alpha for retinal diseases: current knowledge and future concepts. J Ophthalmic Vis Res 2012; 7(1):39–44.
29. Tuominen IS, Tervo TM, Teppo AM, Valle TU, Gronhagen-Riska C, Vesaluoma MH. Human tear fluid PDGF-BB, TNF-alpha and TGF-beta1 vs corneal haze and regeneration of corneal epithelium and subbasal nerve plexus after PRK. Exp Eye Res 2001; 72:631–41.
30. Carreño EA, Enríquez-de-Salamanca M, Tesón C, García- Vázquez G, Stern ME, Whitcup SM, et al. Cytokine and chemokine levels in tears from healthy subjects. Acta Ophthalmol 2012; 88:e250–8.
31. Yamaguchi T, Calvacanti BM, Cruzat A, Qazi Y, Ishikawa S, Osuka A, et al. Correlation between human tear cytokine levels and cellular corneal

changes in patients with bacterial keratitis by *in vivo* confocal microscopy. Invest Ophthalmol Vis Sci 2014; 55(11):7457–66.
32. van de Veerdonk FL, Netea MG, Dinarello CA, Joosten LA. Inflammasome activation and IL-1beta and IL-18 processing during infection. Trends Immunol 2011; 32(3):110–6.
33. Mahajan A, Hasíkováab L, Hampelc U, Grünebooma A, Shana X, Herrmann I, et al., Aggregated neutrophil extracellular traps occlude Meibomian glands during ocular surface inflammation. Ocul Surf 2021; 20:1–12.
34. Kopp EB, Ghosh S. NF-kappa B and rel proteins in innate immunity. AdvImmunol 1995; 58:1–27.
35. Xue ML, Thakur A, Willcox M. Gene expression of pro-inflammatory cytokines and chemokines in mouse eye infected with *Pseudomonas aeruginosa*. Clin Exp Ophthalmol 2002; 30:196–9.
36. AL-Rubaey NK, AL-Tahab AAL, Al-Mola GA. Rapid identification of human adenoviruses and cytokine estimation among patients with epidemic Kerato conjunctivitis in Babylon Governorate, Iraq. Aust J Basic Appl Sci 2017; 11(14):25–9.
37. Konstantopoulos A, Cendra MM, Tsatsos M, Elabiary M, Christodoulides M, Hossain P. Morphological and cytokine profiles as key parameters to distinguish between Gram-negative and Gram-positive bacterial keratitis. Sci Rep 2020; 10:Article number: 20092.
38. Kishazi E, Dor M, Eperon S, Oberic A, Turck N, Hamedani M. Differential profiling of lacri ny SJ. Antibiotic sensitivity pattern of pathogenic bacteria isolated from eyes infection. Biochem Cell Arch 2021; 21:2579–84. Available via https://connectjournals.com/03896.2021.21.2579
39. AL-Maamori AMK, AlSultany SJ. Antibiotic sensitivity pattern of pathogenic bacteria isolated from eyes infection. Biochem Cell Arch 2021; 21:2579–84. Available via https://connectjournals.com/03896.2021.21.2579
40. Ramos MF, Teixeira L, Brandt CR, Auyeung-Kim D. OcularImmunopathology. In: Parker G (ed.). Chapter 14 Immunopathology in toxicology and drug development, molecular and integrative toxicology, Humana Press, Cham, Switzerland, 2017; doi:10.1007/978-3-319-47385-7_14
41. Engelbrecht C, Sardinha LR, Rizzo LV. Cytokine and chemokine concentration in the tear of patients with age-related cataract. Curr Eye Res 2020; 1460–2202.
42. Zheng Y, Rao Y, Li J, Huang Y, Zhao P, Li J. Age-related pro-inflammatory and pro-angiogenic changes in human aqueous humor. Int J Ophthalmol 2018;11(2):196–200.
43. Al-Sultany SJ, Jassim YA. Physiological and immunological effect of lipopolysaccharide of *Escherichia coli* was extracted by hot phenol-water in rabbits. Res J Pharmaceut Biol Chem Sci 2016; 7(3):1530–5.