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Effect of natural antioxidants and important herbal medicines on blood infections and sepsis: A systematic review

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ABSTRACT

Phytochemical and pharmaceutical studies have shown that medicinal plants are rich sources of antioxidant and biologically active compounds. The medicinal plants can have inhibitory effects on various types of parasitic diseases, microbial infections, blood infections, and sepsis. This review was done to report important medicinal plants effective on the prevention and treatment of blood infections and sepsis. Based on the results obtained from the review of numerous articles, indexed in the databases *Information Sciences Institute*, *Scopus*, *PubMed*, and *Google Scholar* etc., the most important medicinal plants effective in the treatment and prevention of sepsis and parasitic, microbial, and viral blood infections are *Veronica officinalis*, *Allium sativum*, *Paeonia lactiflora*, *Angelica Sinensis*, *Hippophae rhamnoides*, *Melissa officinalis*, *Ziziphus Spina-Christi*, *Astragalus species*, *Salvia miltiorrhiza*, *Rheum palmatum*, *Sophora flavescens*, *Scutellaria species*, *Phyllanthus amarus*, *Calendula officinalis*, *Scrophularia striata*, *Lawsonia inermis*, *Artemisia species*, and *Plantago major*. Sterolic, luteolin, tannins, quercetin, saponins and some other bioactive ingredients are the most important bioactive compounds and flavonoids of these medicinal plants that may be used in producing new anti-blood infections and anti-sepsis drugs.



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INTRODUCTION

Blood infections are caused due to infection-induced influence on the immune response. This infection in most cases is caused by a bacterium, but it can also occur by other agents such as fungi, viruses or parasites (Hellman 2015; Rhodes *et al.*, 2017; Ke *et al.*, 2017). In ICU patients, the incidence of sepsis is very variable, and their mortality rate

is from 20% for sepsis, up to 40% for severe sepsis and up to 60% for septic shock. Different microbes such as bacteria, viruses, parasites or fungi can lead to the development of severe infections that can lead to blood infections. In newborns and infants, the causative agents of this condition are usually bacteria. An acute blood infection is referred to as sepsis. In fact, sepsis is a dangerous disease in which the body struggles with a severe infection that spreads through the bloodstream (Gotts and Matthay 2016; Levy *et al.*, 2019). Diseases such as lung infection, bladder infection, kidney infection (Hadian *et al.*, 2018), skin infections, abdominal infections (such as appendicitis), bone infection and brain infections (such as meningitis) can also lead to sepsis in the body. Infections that develop after surgery can also lead to sepsis. Due to the increased use of antibiotics for diseases that are viral and do not require antibiotics, many bacteria have acquired resistance to antibiotics. This

has made it difficult to treat blood infection. When blood infection is difficult to be treated, it leads to death (Jin and Pan 2017; Mohseny *et al.*, 2018). Sepsis, severe sepsis, and septic shock are used to describe the body's response to infection. Systemic inflammatory response syndrome (SIRS) is a systemic response that is characterized by fever, tachycardia, and leukocytosis, which is briefly referred to as SIRS. When SIRS occurs in a patient with suspected infection, he/she contracts sepsis (Hartman *et al.*, 2013; Singer *et al.*, 2017; Seymour *et al.*, 2016). If hypotension in response to fluids or dysfunction of the organs farther from the site of infection occurs, severe sepsis is developed, and if the acidosis of lactic acid, impairment of blood supply to the vital organs of the body, or hypotension without response to fluids occurs, septic shock is developed. The incidence of sepsis has increased over the past 15 years (Hartman *et al.*, 2013; Rhodes *et al.*, 2016). One of the complications and problems associated with sepsis is the imbalance of antioxidant defense system and the level of oxidative stress in the body, both of which occur in sepsis and lead to oxidative stress (Bozza *et al.*, 2013; Gelain *et al.*, 2011; von Dessauer *et al.*, 2011). Medicinal plants have antioxidant activities and can balance the antioxidant defense system (Hosseini *et al.*, 2017; Mohsenzadeh *et al.*, 2016; Kooti *et al.*, 2014). The present review was done to report important effective medicinal plants for the prevention and treatment of blood infections and sepsis.

Based on our literature search, the most important medicinal plants that were addressed in this review are somehow effective in treating and preventing sepsis and parasitic, microbial and viral blood infections (Table 1). Certain medicinal plants such as *Veronica officinalis*, *Allium sativum*, *Paeonia lactiflora*, *Angelica sinensis*, *Hippophae rhamnoides*, *Melissa officinalis*, *Ziziphus spinachristi*, *Astragalus species*, *Salvia miltiorrhiza*, *Rheum palmatum*, *Sophora flavescens*, *Scutellaria species*, *Phyllanthus amarus*, *Calendula officinalis*, *Scrophularia striata*, *Lawsonia inermis*, *Artemisia species*, and *Plantago major* are effective for the prevention and treatment of these diseases.

Veronica officinalis

This plant is from the Plantaginaceae family and is commonly called gypsyweed. Total alcoholic extract, if administered at 10 ml/kg per day, is effective in improving kidney function and creatinine clearance, reducing the pro-inflammatory chemical mediators in the lung such as IL-8 and IL-6, and inhibiting prostaglandin 2 and COX-2 expression by responding to inflammatory stimuli via mitogen-activated protein kinase or NF-kB (Gouveia *et al.*, 2016).

Allium sativum

This plant is from the Amaryllidaceae family and is commonly called garlic. Methanolic garlic extract inhibits TNF α induced by LPS in macrophages. Its active ingredient is sucrose methyl 3-formyl-4-methyl pentanoate (SMFM) that at a dose of 200 μ g/ml, has antiseptic activity, increases bactericidal activity, inhibits leukocyte apoptosis in the spleen and pro-inflammatory cytokines, and can also inhibit damage and inflammation of the lung by its bactericidal properties, and block the production of pro-inflammatory cytokines such as TNF- α , IL-6, IL-1 β (Lee *et al.*, 2015).

Paeonia lactiflora

This plant is from the Paeoniaceae family and is commonly called garden peony. The root of this plant at a dose of 100mg/ml inhibits the uncontrolled release of inflammatory mediators, reduction of excessively intrinsic immune responses, reduction of the relationship of inflammation and coagulation, and protection of endothelial cells effective on the brain that are used to treat brain disorders in people with sepsis (Zhang *et al.*, 2018).

Angelica Sinensis

This plant belongs to the Apiaceae family and is commonly called Dong Quai. Aqueous extract - daily 5-50 g - for each individual with a mean weight of 75 kg reduces the endotoxin-induced release of HMGB1 in macrophage environment through involving in cytoplasmic translocation and reducing the induction of the release of inflammation-mediating endotoxins such as nitric oxide and TNF. It is also effective on macrophages (Wang *et al.*, 2006).

Hippophae rhamnoides

This plant is from the Elaeagnaceae family and is commonly called sea buckthorn. The ethanolic extract from the leaves of this plant at a dose of 50 mg/ml is effective on macrophages isolated from the blood. This plant has an antiviral property that is due to decreased TNF-a and increased IFN- γ (Jain *et al.*, 2008).

***Melissa officinalis* (Lemon balm)**

This plant is from the Lamiaceae family and is commonly called balm. Ethanolic extract of its leaf at a dose of 100 mg/kg, is effective on sepsis-induced infectious disorders in rodents (Eudes Filho *et al.*, 2017).

Table 1374: The most important medicinal plants effective in the treatment and sepsis and parasitic, microbial, and viral blood infections

Scientific name	Active ingredients	Plant figure
<i>Veronica officinalis</i>	phenolic, sterolic, luteoline, hispid (Gouveia <i>et al.</i> , 2016)	
<i>Allium sativum</i>	sucrose methyl 3-formyl-4-methylpentanoate (SMFM) (Le <i>et al.</i> , 2015)	
<i>Paeonia lactiflora</i>	Cis-epsilon-viniferin, trans-resveratrol, trans-resveratrol-4'-O-beta-D-glucopyranoside, trans-epsilon-viniferin (Zhang <i>et al.</i> , 2018)	
<i>Angelica sinensis</i>	Phytosterols, ligustilide, butylphthalide, p-cymene, ferulate, flavonoids (Wang <i>et al.</i> , 2006)	
<i>Hippophae rhamnoides</i>	Flavonols, phenolic acids, quercetin (Jain <i>et al.</i> , 2008)	
<i>Melissa officinalis</i>	tannins, terpenes, α -humulene, β -bourbonene (Eudes Filho <i>et al.</i> , 2017)	

Ziziphus spina-christi

This plant is from the Rhamnaceae family and is commonly called Christ's thorn jujube. It contains flavonoids (quercetin) and saponin, such as betulinic acid and triterpenoid saponin, has antibac-

terial and antiviral properties. The methanolic extract of its leaves at 100, 200, or 300 mg/kg prevents liver and spleen damage and reduces the inflammatory mediators and cytokines, and the oxidative stress, and increases the antioxidant defense system, catechin, epicatechin, epigallocatechin, and gallic acid, present in this plant, have

Table 1375: The most important medicinal plants effective in the treatment and prevention of sepsis and parasitic, microbial, and viral blood infections (Contd....)

Scientific name	Active ingredients	Plant figure
<i>Ziziphus spina-christi</i>	Quercetin, saponin, betulinic acid (Dkhil <i>et al.</i> , 2018)	
<i>Astragalus</i>	Isoflavonoids and Astragalosides (Cui <i>et al.</i> , 2010)	
<i>Salvia miltiorrhiza</i>	tanshinone I, tanshinone IIA (Cui <i>et al.</i> , 2010)	
<i>Rheum palmatum</i>	rutin, ferulic acid, α -tocopherol (Cui <i>et al.</i> , 2010)	
<i>Sophora flavescens</i>	Oxymatrine (Cui <i>et al.</i> , 2010)	

the potent anti-inflammatory and hepatoprotective effects. Some of its compounds are involved in the NF- κ B and MAPK pathways. It also inhibits TNF α and IL-1 β in the liver and spleen by inhibiting translocation of NF- κ B from the cytoplasm into the nucleus (Dkhil *et al.*, 2018).

Astragalus species

This plant is from the Fabaceae family and is commonly called Milkvetch. *Radix astragali* (Huangqi) is derived from the root of *Astragalus membranaceus*. It is useful for the treatment of immune disorders and liver diseases. The plant contains flavonoids and saponin, and the active ingredients in its

Table 3: The most important medicinal plants effective in the treatment and prevention of sepsis and parasitic, microbial, and viral blood infections (Contd....)


Scientific name	Active ingredients	Plant figure
<i>Scutellaria</i>	Wogonin (Cui <i>et al.</i> , 2010)	
<i>Phyllanthus amarus</i>	Alkaloids, flavonoids, lactones, steroids, triterpenes, lignans, tannins (Cui <i>et al.</i> , 2010)	
<i>Calendula officinalis</i>	flavonol glycosides, saponins, sesquiterpene glucoside (Maspi <i>et al.</i> , 2010)	
<i>Scrophularia striata</i>	Scrophuloside A, Harpagoside B, 5-hydroxyloganin, 8-O-acetylharpagide, Verbascoside (Naserifard <i>et al.</i> , 2013)	
<i>Lawsonia inermis</i>	quercetin and lalioside (Behdani <i>et al.</i> , 2009)	

extract inhibits the secretion of HBsAg and HBeAg at 100 µg/mL and HBsAg at 120 mg/kg and is, therefore, effective to treat chronic viral hepatitis and septicemia (Cui *et al.*, 2010).

Salvia miltiorrhiza

This plant is from the Lamiaceae family and is commonly called Chinese sage. Both hydrophilic and hydrophobic fractions of this plant have biological

Table 4: The most important medicinal plants effective in the treatment and prevention of sepsis and parasitic, microbial, and viral blood infections (Contd....)

Scientific name	Active ingredients	Plant figure
<i>Artemisia</i>	Santonin, Artemisinin, Scopoletin (Sun <i>et al.</i> , 2006)	
<i>Plantago major</i>	allantoin, aucubin, ursolic acid, flavonoids, asperuloside (Akinyemi <i>et al.</i> , 2005)	

effects; its aqueous solution inhibits HBV secretion with an IC₅₀ of 4.17 µg/ml and suppresses the expression of HBsAg and HBeAg with an IC₅₀ of 3.94 at 2.46 µg/mL (Cui *et al.*, 2010).

Rheum palmatum

This plant is from the Polygonaceae family and is commonly called rhubarb. The extract of this plant is used to treat gastroenteritis and liver disease. It can also inhibit coxsackievirus and herpes simplex virus, and its oil inhibits expression of HBV Ag (HBsAg and HBeAg).

The aqueous extract of this plant reduces HBV concentration and inhibits the secretion of HBsAg and HBV DNA polymerase activity, and has an antiviral effect against hepatitis B virus.

The ethanolic extract also inhibits the production of HBV DNA and the expression of HBsAg in a dose-dependent manner. Its active ingredient is chrysophanol 8-O-β-Dglucoside that with an IC₅₀ of 36.98 µg/mL and at 237.4 µg/mL, exhibits activity against HBV DNA production (Cui *et al.*, 2010).

Sophora flavescens

This plant is from the Fabaceae family and is commonly called sophora. Oxymatrine is an alkaloid isolated from the root of *Sophora flavescens* that has antiviral, antifibrotic, hepatoprotective, and immunomodulatory activities, especially against HBV. Oxymatrine at 1,000 µg/mL inhibits the production of HBV DNA and secretion of HBsAg and HBeAg. It also reduces the concentration of intrahepatic HBsAg, HBeAg and HBcAg in transgenic mice and results in the negativity of intrahepatic HBsAg, HBeAg and HBcAg at a dose of 200 mg/kg treated for 30 days (Cui *et al.*, 2010).

Scutellaria species

This plant is from the Lamiaceae family and is commonly called skullcaps. Wogonin is a non-flavonoid derived from this plant used to treat inflammation and infectious diseases, has antiviral activity, suppresses HBsAg secretion with IC₅₀ of 4 µg/mL, reduces HBV DNA levels, and inhibits the DHBV DNA polymerase with IC₅₀ of 0.57 µg/mL (Cui *et al.*, 2010).

Phyllanthus species

This plant is from the Phyllanthaceae family and is commonly called a stone breaker. The ethanolic extract of this plant affects chronic kidney disease and serves as an antiviral at a concentration of 100 µg/ml, and has an IC₅₀ of 50 for HBsAg greater than 200 µg/ml. It contains compounds such as alkaloids, flavonoids, lactones, steroids, triterpenes, lignans, and tannins. The ethanolic extract of this plant produces suppressive effects on the secretion of HBsAg, the expression of HBsAg mRNA, and the proliferation of HBV, thereby treating the viral infection of the blood (Cui *et al.*, 2010).

Calendula officinalis

This plant is from the Asteraceae family and is commonly called marigold. The extract of this plant at a concentration of 500 mg/ml reduced all parasites and at low concentrations, LD₅₀ of 17 mg/ml for alcoholic extract and 215 mg/ml for aqueous extract, exhibited anti-leishmania and antiparasitic activities that reduce parasitic infection of the blood (Maspi *et al.*, 2010).

Scrophularia striata

This plant is from the Scrophulariaceae family and is commonly called Snapdragon. At the concentration of 10 mg/ml, the drug was controlled, and at

the concentration of 25 mg/ml of the extract, on the third day, the complete elimination of *L. major amastigotes* in macrophages occurred. The percentage of contaminated macrophages is decreased by increasing the concentration of the extract, thereby reducing the parasitic infection in the bloodstream and subsequently reducing sepsis (Naserifard *et al.*, 2013).

Lawsonia inermis

This plant is from the Lythraceae family and is commonly called Hina, and the aqueous and ethanolic extracts of the leaves of this plant exhibit a wide range of antimicrobial properties, so that the hina ethanolic and aqueous extracts were used against *S. aureus* bacteria. The MICs of the aqueous and ethanolic extracts were obtained 2.5 and 3 mg/ml, respectively. The aqueous extracts at 7.5 mg/ml can inhibit the growth of all 25 isolates of *S. aureus*. The ethanolic extract at 7.5 mg/ml prevents the growth of all isolates of *S. aureus* (Behdani *et al.*, 2009).

Artemisia species

This plant belongs to the Asteraceae family and is commonly called mugwort. It is effective for the treatment of rheumatoid arthritis, dermatitis and sepsis. This plant inhibits TNF- α release by stimulating macrophage LPS by regulating the activity of MAPK and NF- κ B. The ethanolic extract at 150-300 mg/kg protects the body against lethal endotoxins and suppresses the expression of TNF- α mRNA in the liver and lungs. It also inhibits expression of TNF- α , IL-1 β and COX-2, and phosphorylation of MAPK, and also inhibits the activity of NF- κ B and phosphorylation of I κ B α (Sun *et al.*, 2006).

Plantago major

Which is Plantaginaceae family with the generic name of the larger plantain, the highest diameter of the non-growth of the aqueous and ethanolic extracts of large leafy leaves in 80 mg concentration was due to *Staphylococcus aureus*, with a minimum inhibitory concentration of aqueous plaque extract for *Staphylococcus aureus* 25 mg/ml, for ethanolic extract, it was 12.5 mg/ml. The minimum bactericidal concentrations of aqueous and ethanolic extracts for *S. aureus* were obtained 50 and 25 mg/ml (Akinyemi *et al.*, 2005).

Turmeric, lemon, green tea, garlic, oak, and rosemary are the other medicinal plants that have been reported to be effective on blood infections and sepsis.

Turmeric is known as one of the traditional and herbal drugs for various types of health issues, including blood infections. Curcumin present in turmeric is very suitable for increasing blood protein levels. Increasing blood protein in the body can

stop various types of infections. Turmeric is also very useful to prevent inflammation (Niranjan and Prakash 2008; Prasad and Tyagi 2015; Yang *et al.*, 2013).

Lemon is a rich source of vitamin C, which can be very effective in the treatment of blood infections. Lemon boosts the immune function of the body. It also inhibits the growth of bacteria and helps detoxify the blood (Briggs 2018; Mshelia 2018).

Research has demonstrated green tea is very effective in treating blood infections. Green tea has compounds that can inhibit bacteria (Li *et al.*, 2012; Wheeler *et al.*, 2007).

Garlic is one of the best vegetables that can be widely used to treat many diseases. It is also one of the most suitable treatments for blood infections because it contains a substance called allicin that fights the infectious and toxic bacteria of the blood. It also greatly boosts the immune system (Ayaz and Alpsoy 2007; Bakri and Douglas 2005; Salman *et al.*, 1995).

Oak has highly potent antioxidant and antibacterial properties. The palm and leaves of the oak tree contain tannins, malic acid, quercetin, pectin, resin and oil. It exerts strong effects on the reduction and treatment of bacterial and infectious diseases (Chahardooli and Khodadadi 2014; Deryabin *et al.*, 2015).

Rosemary is an anti-inflammatory and antibacterial plant and is there used in the treatment of various types of infections. The easiest way to use rosemary properties is to use its essential oil (Luqman *et al.*, 2007; Jiang *et al.*, 2011; Issabeagloo *et al.*, 2012; Ojeda-Sana *et al.*, 2013).

The most important bioactive compounds and flavonoids of these medicinal plants that are effective on sepsis include sterolic, luteoline, sucrose methyl 3-formyl-4-methylpentanoate (SMFM), Cis-epsilon-viniferin, trans-resveratrol, trans-resveratrol-4'-O-beta-D, glucopyranoside, trans-epsilon-viniferin, phytosterols, ligustilide, butylphthalide, tannins, terpenes, α -humulene, β -bourbonene, quercetin, saponin, betulinic acid, isoflavonoids, astragalosides, tanshinone I, tanshinone IIA, rutin, ferulic acid, α -tocopherol, oxymatrine, wogonin, alkaloids, lactones, steroids, triterpenes, lignans, tannins, sesquiterpene glucoside, scrophuloside A, allantoin, aucubin, ursolic acid, asperuloside etc.

Sepsis actually occurs when the primary responsibility of the host is reinforced by an infection and ultimately is dysregulated. This leads to an imbalance between the pro-inflammatory responses and the anti-inflammatory responses. In physiological conditions, there is a balance between the formation of oxidative species and their elimination

by antioxidant compounds (Lorente *et al.*, 2015; Nagar *et al.*, 2018). Oxidative stress is caused when this balance is disturbed by the production of a large amount of ROS free radicals or the weakness of the antioxidant defense system. The use of medicinal herbs and natural antioxidants has the greatest therapeutic effects on the antioxidant system and elimination of free radicals (ROS and NOS) (Moradi *et al.*, 2018; Naserifar *et al.*, 2017; Tajallaie-Asl *et al.*, 2017).

The presence of phenolic and antioxidant compounds in various organs of these medicinal plants cause strong antioxidant, anti-inflammatory, antispasmodic, antiseptic and antimicrobial effects (Parsaei *et al.*, 2016; Rouhi-Boroujeni *et al.*, 2016; Van Vuuren 2008). Actually, medicinal plants introduced in this review can be used as complementary medicines because of the presence of antimicrobial and antiviral compounds, bioactive ingredients, phenols, flavonoids, etc.

CONCLUSION

Medicinal plants and natural antioxidants can have antimicrobial, antiviral and antiparasitic effects due to bioactive ingredients and strong antioxidants that they produce, and therefore can be used as natural antibacterial drugs. The results of our review indicated that the function of these plants might be due to their active compounds and active flavonoids such as tannins, terpenes, α -humulene, β -bourbonene, quercetin, saponin, betulinic acid, isoflavonoids, allantoin, aucubin, ursolic acid, asperuloside etc. In the clinical trials, these have to be evaluated on blood infections and sepsis to can be considered new candidates for producing effective drugs.

Authors' contributions

All authors all contributed equally in planning and carrying out this study. All authors read the manuscript and confirmed the publication for the final version.

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REFERENCES

Akinyemi KO, Oladapo O, Okwara CE, Ibe CC, and Fasare KA, 2005. Screening of crude extracts of six medicinal plants used in South-West Nigerian unorthodox medicine for anti-methicillin resistant *Staphylococcus aureus* activity. *BMC Complement. Altern. Med.* 5(1): 6.

Ayaz E, and Alpsy HC, 2007. Garlic (*Allium sativum*) and traditional medicine. *Acta Parasitol. Turc.* 31(2): 145-9.

Bakri IM, and Douglas CWI, 2005. Inhibitory effect of garlic extract on oral bacteria. *Arch. Oral Biol.* 50(7): 645-651.

Behdani M, Ghazvini K, Mohammadzadeh AR, and Sadeghian A, 2009. Antibacterial activity of Henna extracts against *Staphylococcus aureus* and *Pseudomonas aeruginosa*. *Horizon Med. Sci.* 15(2): 46-51.

Bozza FA, D'Avila JC, Ritter C, Sonnevile R, Sharsar T, Dal-Pizzol F, 2013. Bioenergetics, mitochondrial dysfunction, and oxidative stress in the pathophysiology of septic encephalopathy. *Shock.* 39: 10-16.

Briggs M, 2017. Vitamin C and infectious disease: a review of the literature and the results of a randomized, double-blind, prospective study over 8 years. *Recent Vitam. Res.* CRC Press. 45-88.

Chahardooli M, and Khodadadi E, 2014. The Biosynthesis of Silver Nanoparticles using OAK fruit extract and the investigation of their Anti-Microbial Activities against nosocomial infection agents. *J. Ilam Univ. Med. Sci.* 22 (4) :27-33.

Cui X, Wang Y, Kokudo N, Fang D, and Tang W, 2010. Traditional Chinese medicine and related active compounds against hepatitis B virus infection. *Biosci Trends.* 4(2): 39-47.

Deryabin Dmitry G, and Tolmacheva Anna A, 2015. Antibacterial and anti-quorum sensing molecular composition derived from quercus cortex (oak bark) extract. *Molecules.* 20(9): 17093-17108.

Dkhil MA, Al-Quraishy S, and Moneim AEA, 2018. *Ziziphus spina-christi* leaf extract pretreatment inhibits liver and spleen injury in a mouse model of sepsis via anti-oxidant and anti-inflammatory effects. *Inflammopharmacology.* 26(3): 779-791.

Eudes Filho J, Silveira D, Soares AIC, Carneiro FP, de Assis MS, Leite FB, *et al.*, 2017. Effects of lemon balm (*Melissa officinalis*) on behavioral deficits and memory impairment of rats surviving sepsis. *J. Med. Plants Res.* 11(8): 153-160.

Gelain DP, de Bittencourt Pasquali, MA, Comim CM, Grunwald MS, Ritter C, Tomasi CD, *et al.*, 2011. Serum heat shock protein 70 levels, oxidant status, and mortality in sepsis. *Shock.* 35(5): 466-470.

Gotts JE, and Matthay MA, 2016. Sepsis: pathophysiology and clinical management. *Br. Med. J.* 353: i1585.

- Gouveia EHH, Júnio RFGR, Brito MVH, Yasojima EY, Silva AMF, Monteiro AM, *et al.*, 2016. Effects of Veronica Officinalis extract in the kidney of rats with induced sepsis. *Int. Arch. Med.* 9 (319).
- Hadian B, Zafar-Mohtashami A, and Ghorbani F, 2018. Study of urine composition of patients with recurrent nephrolithiasis in Lorestan, Iran. *Iranian J. Kidney Dis.* 12: 22-26.
- Hellman J, 2015. Addressing the complications of Ebola and other viral hemorrhagic fever infections: using insights from bacterial and fungal sepsis. *PLoS Pathog.* 11(10): e1005088.
- Hosseini Z, Lorigooini Z, Rafieian-Kopaei M, Shir-mardi H, and Solati K, 2017. A review of botany and pharmacological effect and chemical composition of Echinophora species growing in Iran. *Pharmacogn. Res.* 9(4):305-12.
- Issabeagloo E, Kermanizadeh P, Taghizadieh M, Forughi R, 2012. Antimicrobial effects of rosemary (Rosmarinus officinalis L.) essential oils against Staphylococcus spp. *Afr. J. Microbiol. Res.* 6(23):5039-42.
- Jain M, Ganju L, Katiyal A, Padwad Y, Mishra KP, Chanda S, *et al.*, 2008. Effect of Hippophae rhamnoides leaf extract against Dengue virus infection in human blood-derived macrophages. *Phytomedicine.* 15(10): 793-799.
- Jiang Y, Wu N, Fu YJ, Wang W, Luo M, Zhao CJ, *et al.*, 2011. Chemical composition and antimicrobial activity of the essential oil of Rosemary. *Environmen. Toxicol. Pharmacol.* 32(1):63-8.
- Jin B, and Pan G, 2017. The susceptibility of infection site in sepsis. *Chin. Pediatr. Emerg. Med.* 24(7): 504-506.
- Ke Q, Weaver W, Pore A, Gorgoglione B, Wildschutte JH, Xiao P, *et al.*, 2017. Role of viral hemorrhagic septicemia virus matrix (M) protein in suppressing host transcription. *J Virol.* JVI-00279.
- Kooti W, Ghasemiboroon M, Asadi-Samani M, Ahangarpour A, Zamani M, Amirzargar A, *et al.*, 2014. The effect of Halcoholic extract of celery leaves on the delivery rate (fertilization and stillbirths), the number, weight and sex ratio of rat offspring. *Adv. Environ. Biol.* 8(10):824-30.
- Kooti W, Moradi M, Ali-Akbari S, Sharafi-Ahvazi N, Asadi-Samani M, and Ashtary-Larky D, 2015. Therapeutic and pharmacological potential of Foeniculum vulgare Mill: A review. *J. Herbmed Pharmacol.* 4(1):1-9.
- Lee SK, Park YJ, Ko MJ, Wang Z, Lee HY, Choi YW, and Bae YS, 2015. A novel natural compound from garlic (Allium sativum L.) with therapeutic effects against experimental polymicrobial sepsis. *Biochem. Biophys. Res. Commun.* 464(3): 774-779.
- Levy MM, Rhodes A, Evans LE, Antonelli M, Bailey H, Kesecioglu J, *et al.*, 2019. Counterpoint: Should the surviving sepsis campaign guidelines be retired? *No. Chest.* 155(1): 14-17.
- Li W, Zhu S, Zhang Y, Li J, Sama AE, Wang P, and Wang H, 2012. Use of animal model of sepsis to evaluate novel herbal therapies. *J. Vis. Exp.* 62: pii: 3926.
- Lorente L, Martín MM, Almeida T, Abreu-González P, Ferreres J, Solé-Violán J, 2015. Association between serum total antioxidant capacity and mortality in severe septic patients. *J. Crit. Care.* 30(1): 217-e7.
- Luqman S, Dwivedi GR, Darokar MP, Kalra A, Khanuja SP, 2007. Potential of rosemary oil to be used in drug-resistant infections. *Altern. Ther. Health Med.* 13(5):54-9.
- Maspi N, Ghafarifar F, Bahrami AM, Bastaminejad S, and Shamsi M, 2010. Evaluation of the leishmanicidal effect of watery & ethanolic flowers calendula Officinalis extracts on promastigotes of leishmania major (MRHO/IR/75/ER) in Vitro. *J. Ilam Univ. Med. Sci.* 18(1): 28-33.
- Mohseny AB, van Velze V, Steggerda SJ, Smits-Wintjens VE, Bekker V, and Lopriore E, 2018. Late-onset sepsis due to urinary tract infection in very preterm neonates is not uncommon. *Eur. J. Pediatr.* 177(1): 33-8.
- Mohsenzadeh A, Ahmadipour S, Ahmadipour S, and Asadi-Samani M, 2016. Iran's medicinal plants are effective on fever in children: A review. *Der Pharm. Lett.* 8(1):129-34.
- Moradi B, Abbaszadeh S, Shahsavari S, Alizadeh M, and Beyranvand F, 2018. The most useful medicinal herbs to treat diabetes. *Biomed. Res. Ther.* 5(8): 2538-51.
- Mshelia BM, 2018. The antibacterial activity of honey and lemon juice against Streptococcus pneumoniae and Streptococcus pyogenes isolates from respiratory tract infections. *Acta Sci. Microbiol.* 1: 22-7.
- Nagar H, Piao S, and Kim CS, 2018. Role of mitochondrial oxidative stress in sepsis. *Acute Crit. Care.* 33(2): 65-72.
- Naserifar R, Bahmani M, Abdi J, Abbaszadeh S, Nourmohammadi G-A, and Rafieian-Kopaei M, 2017. A review of the most important native medicinal plants of Iran effective on leishmaniasis according to Iranian ethnobotanical references. *Int. J. Adv. Biotechnol. Res.* 8(2): 1330-6.

- Naserifard R, Dalimi Asl A, and Ahmadi N, 2013. Influence of aqueous extract *Scophularia straiata* on the growth of *Leishmania major* in mice peritoneal macrophages (BALB/c). *Res. Med.* 36(5): 12-8.
- Niranjan A, and Prakash D, 2008. Chemical constituents and biological activities of turmeric (*Curcuma longa* L.)-a review. *J. Food Sci. Technol.* 45(2): 109.
- Ojeda-Sana AM, van Baren CM, Elechosa MA, Juárez MA, and Moreno S, 2013. New insights into antibacterial and antioxidant activities of rosemary essential oils and their main components. *Food Control.* 31(1):189-95.
- Parsaei P, Bahmani M, Naghdi N, Asadi-Samani M, Rafieian-Kopaei MM, and Boroujeni S, 2016. Shigellosis phytotherapy: A review of the most important native medicinal plants in Iran effective on *Shigella*. *Der Pharm. Lett.* 8(2):249-55.
- Prasad S, and Tyagi AK, 2015. Curcumin and its analogues: a potential natural compound against HIV infection and AIDS. *Food Func.* 6(11): 3412-9.
- Rhodes A, Evans LE, Alhazzani W, Levy MM, Antonelli M, Ferrer R, *et al.*, 2017. Surviving sepsis campaign: international guidelines for the management of sepsis and septic shock: 2016. *Intensive Care Med.* 43(3): 304-77.
- Rouhi-Boroujeni H, Asadi-Samani M, and Moradi MT, 2016. A review of the medicinal plants effective on headache based on the ethnobotanical documents of Iran. *Der Pharm. Lett.* 8(3):37-42.
- Salman H, Bergman M, Bessler H, Punskey I, Djaldetti M, 1999. Effect of a garlic derivative (alliin) on peripheral blood cell immune responses. *Int. J. Immunopharmacol.* 21(9): 589-97.
- Seymour CW, Liu VX, Iwashyna TJ, Brunkhorst FM, Rea TD, Scherag A, *et al.*, 2016. Assessment of clinical criteria for sepsis: for the Third International Consensus Definitions for Sepsis and Septic Shock (Sepsis-3). *JAMA.* 315(8): 762-74.
- Singer M, Deutschman CS, Seymour CW, Shankar-Hari M, Annane D, Bauer M, *et al.*, 2016. The third international consensus definitions for sepsis and septic shock (Sepsis-3). *JAMA.* 315(8): 801-10.
- Sun Y, Li YH, Wu XX, Zheng W, Guo ZH, Li Y, *et al.*, 2006. Ethanol extract from *Artemisia vestita*, a traditional Tibetan medicine, exerts anti-sepsis action through down-regulating the MAPK and NF- κ B pathways. *Int. J. Mol. Med.* 17(5): 957-62.
- Tajallaie-Asl F, Mardani M, Shahsavari S, and Abbaszadeh S, 2017. Menstruation phytotherapy according to Iran ethnobotanical sources. *J. Pharm. Sci. Res.* 9(6): 986-90.
- Van Vuuren SF, 2008. Antimicrobial activity of South African medicinal plants. *J. Ethnopharmacol.* 119(3): 462-72.
- von Dessauer B, Bongain J, Molina V, Quilodrán J, Castillo R, and Rodrigo R, 2011. Oxidative stress as a novel target in pediatric sepsis management. *J. Crit. Care.* 26(1): 103-e1.
- Wang H, Li W, Li J, Rendon-Mitchell B, Ochani M, Ashok M, *et al.*, 2006. The aqueous extract of a popular herbal nutrient supplement, *Angelica sinensis*, protects mice against lethal endotoxemia and sepsis. *J Nutr.* 136(2): 360-5.
- Wheeler DS, Lahni PM, Hake PW, Denenberg AG, Wong HR, Snead C, *et al.*, 2007. The green tea polyphenol epigallocatechin-3-gallate improves systemic hemodynamics and survival in rodent models of polymicrobial sepsis. *Shock.* 28(3): 353-9.
- Yang C, Wu K, Li SH, and You Q, 2013. Protective effect of curcumin against cardiac dysfunction in sepsis rats. *Pharm. Boil.* 51(4): 482-7.
- Zhang N, Cheng C, Olaleye OE, Sun Y, Li L, Huang Y, *et al.*, 2018. Pharmacokinetics-based identification of potential therapeutic Phthalides from Xuebijing, a Chinese herbal injection used in sepsis management. *Drug Metabol. Dispos.* 46(6): 823-34.