

Bioactive Component and their Role in Inhibition of Bacterial Meningitis

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Abstract

Bacterial meningitis is a severe ailment present in the peritoneum, mainly filled with CSF. The characteristic triad of meningitis indications of migraine, high temperature, and dystonia are caused by inflammation of the meninges and submucosa, as well as pleocytosis present in the CSF. The pathogenesis of BM requires complicated pathways involving pathogen survivability and proliferation in the stream, enhanced susceptibility of the Blood Brain Barrier (BBB), oxidative stress, and an overactive provocative response present in the CNS. The pathophysiology of bacterial meningitis has been better understood because to experimental and genetic association investigations. The present review paper summarizes the pathogenesis of invading pathogens and role of different bioactive compounds taken from different plant extracts that might be helpful in curing the diseases. These bioactive compounds might have the inhibitory factor against the emerging disease and this need to be inculcate by performing various methodologies for future investigations.

Keywords: Bacterial meningitis; CSF; Blood brain barrier; Oxidative stress; Bioactive compounds; Inhibitory factors

Introduction

Bacterial meningitis is a acute ailment present in the peritoneum, mainly filled with CSF. It is characterised by migraine, high temperature, and dystonia caused by inflammation of the meninges and submucosa, as well as pleocytosis present in the CSF. Meningitis caused by *S. suis* infection affects 84.6 percent of Europeans and 75.2 percent of Asians, respectively. When compared to significant inflammation or vascular difficulties, brain cortex and parenchyma involvement can result in lifestyle modifications, exact neuropathies, and memory deficits. Bacterial meningitis is a therapeutic catastrophe, and people who have the disease should be evaluated and treated right away [1].

Materials and Methods

Cause of bacterial meningitis

In affluent countries, *Streptococcus pneumoniae* is the mainly prevalent root that causes the disease bacterial meningitis and 75% of its cases has been reported across the globe [2]. *Streptococcus pneumoniae* is a commensal bacterium that lives in healthy people's throat and upper respiratory system. It can, however, spread and establish itself in generally sterile environments such as blood, CSF, and the pleural space, resulting in Invasive Pneumococcal Illness (IPD). In these groups, after *S. pneumoniae*, *Listeria* is the second most prevalent pathogen. Meningitis caused by *L. monocytogenes* has a dismal prognosis, which is contingent on prompt amoxicillin therapy. Pneumococcal meningitis is more prevalent in a person that falls under the age of five as well as those counted above 65, although meningococcal meningitis is more common in grown-up offspring, teenagers, and immature adults [3].

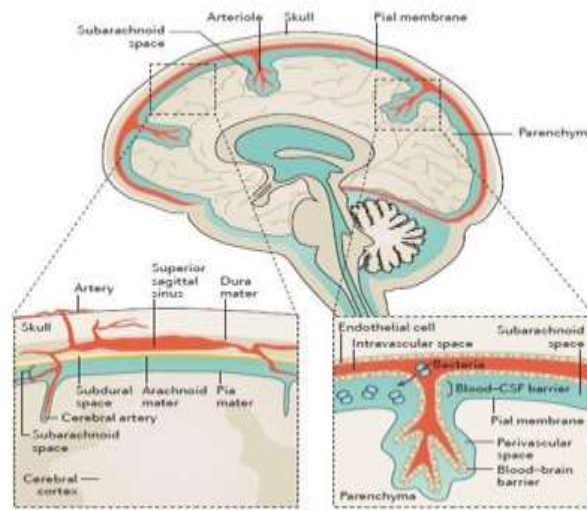


FIG. 1. Anatomical consideration of bacterial meningitis.

Due to reduced transmission of invasive strains, Pneumococcal polysaccharide immunizations, which are widely used in developed nations, have reduced rates of pneumococcal meningitis not just among immunised newborn infants, but also in age demographics that are not eligible for vaccination (herd protection). Severe encephalopathy can be caused by a multitude of microorganisms, or it could be a signal of a non-contagious illness. The most deadly form of the disease is bacterial meningitis; the most typical avenues of infection are respiratory, but it can also be intestinal, as in listerial infection [4].

Mechanism

Bacteria invade the intracranial space via the bloodstream, or contamination can progress from neighbouring sites like the nasal cavities or the coronoid bone present in the inner ear. The most prominent mechanism for bacteria to enter the subarachnoid space is through blood-borne pathogen invasion, which involves epithelial penetration, intrusion, diligence, and replication of microorganisms during the transmission, and subsequently bridging the BBB [5].

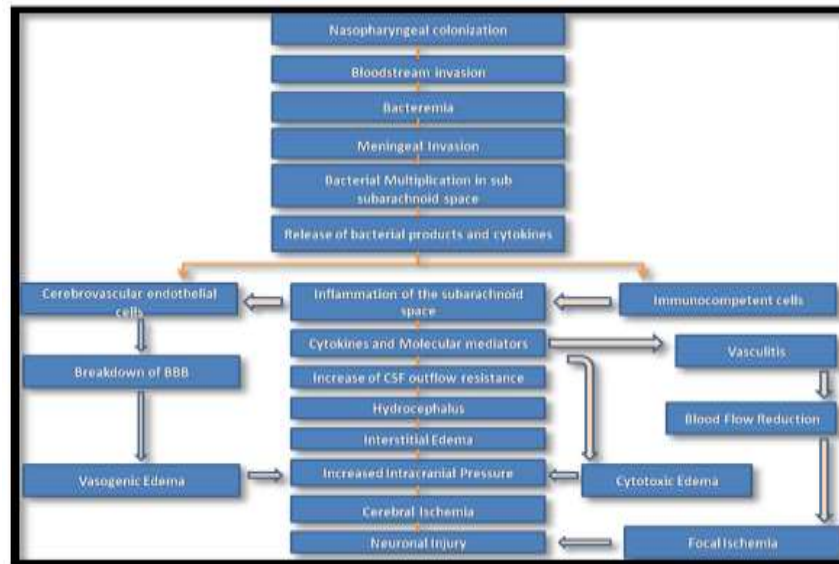


FIG. 2. Mechanism of bacterial meningitis.

Immigration of the host by the pathogen

Before entering the stream, various pathogens infect mucosa surfaces present in the respiratory tract or in the urogenital tract or stomach tract. Fetal asplenia, component deficit, cytotoxic medicine, and antibody inadequacy are all host factors that enhance the chance of meningeal pathogens causing invasive infection [6].

Endurance within the bloodstream

The germs must contend with the bactericidal environment once they enter the bloodstream. Anti-phagocytic capsules made of carbohydrates from *N. meningitidis*, *S. pneumoniae*, *H. influenzae*, group B streptococci, and *E. coli* operate as static shields, preventing the authentication of opsonins over the surface, predominantly to harmonize the factors. Meningococcal capsular polysaccharides can also reduce the amount of C4 binding protein (C4bp) deposited on the complement component's surface, decreasing complement-mediated direct bacterial death. A multitude of bacterial surface chemicals recognise certain supplement components in addition to the capsule, to obstruct counterbalance bacterial eradication [7].

Through components like FH-Binding Protein (FHBP), Neisserial Surface Protein A (NSPA), and porin B, *N. meningitidis* can adhere in a straight line to Factor H (FH), which seems to be the critical factor that operates different activation of complementary pathways. Outer Membrane Protein A (OMPA) is a foremost facade protein present in *E. coli*, imparts conflict to serum bactericidal action by adhering to C4bp, a native suppressor of the classical and lectin pathways [8].

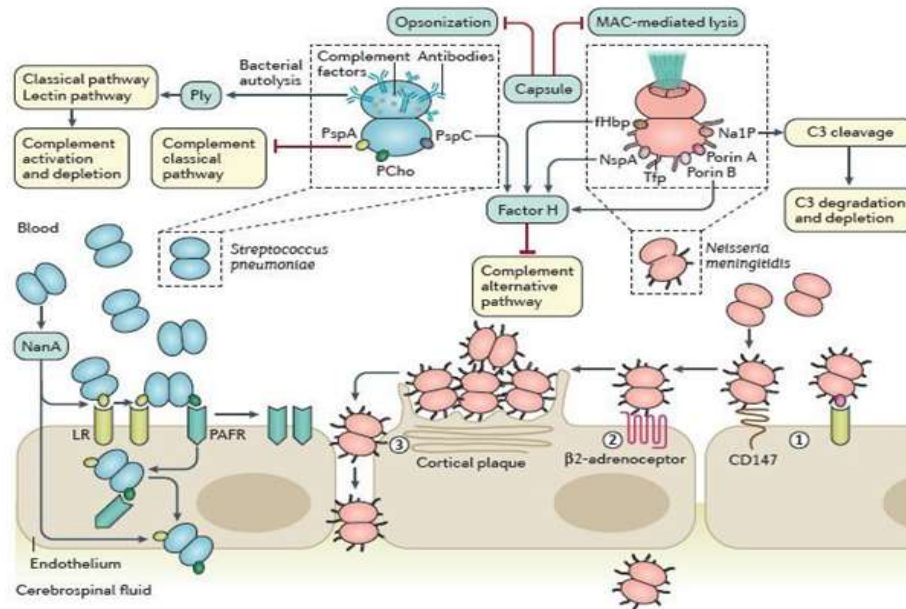


FIG. 3. Microbial determination in the transmission and incursion of the CNS.

Acquiring access to the CNS

Protracted elevated levels of bacteraemia have been established in experimental animals and humans to encourage the penetration of various invading pathogens into the subarachnoid space, presumably by assessing the chances of pathogens communicating with the innermost cells present in the barrier of blood CSF. Bacterial entrance points in the subarachnoid and perivascular regions could be post-capillary venules and veins. Furthermore, post-capillary venules and veins are located in close proximity to the CSF and belong to the 'leaky' section of the brain's vascular tree [9].

Immune activation in bacterial meningitis

Because innate responses in the cortical area tend to be poor at targeting prospective pathogens, infestations are likely to sustain after they penetrate the CSF. The PRRs that are soluble, such as coagulation factors, are lacking, that attach to pathogen surfaces and flag them for phagocytosis, could be to blame for the immunological deficit. Complement deposition can also promote bacterial lysis in sensitive species, such as *Neisseria* spp., by forming a Membrane Attack Complex (MAC). The BBB, essentially acts as a biochemical filter to limit the entry of big macromolecules and immunodeficient cells, prevents blood complement proteins from invading into the CSF. As a response, infections that effectively penetrate the CSF can grow swiftly and achieve high inhabitants in a matter of hours [10].

Therapeutics in bacterial meningitis

Long-term cognitive impairment in bacterial meningitis recipients is mediated by MIF, according to reported in 2021. This suggests that MIF could be a target for immune-modulating supplementary therapy [11]. In a study published in 2022 demonstrated that intracranial heparin-binding glycoprotein is a robust supplementary analytical marker that is superior to lactate and procalcitonin in acknowledging the meningitis infections present in the bloodstream and ventriculitis. In the early stages of inflammation, in response to infections, active neutrophils rapidly recruit and release Heparin-Binding Protein (HBP). As a result, it's a potential biomarker with possible applications in infectious disease diagnostics. HBP was found to be more effective than CSF cytochemical markers in differentiating bacterial meningitis from viral meningitis [12].

Moreover, during the experimental study it was found that CSF NFL level may indeed be a helpful biomarker for bacterial

meningitis prognosis analysis. These biomarkers are helpful in performing a multiplex-PCR technique that is effective, quick, and accurate for the detection of acute bacterial meningitis can greatly enhance the diagnosis in cases where the culture is negative. A variety of biomarkers can be utilised to diagnose the condition depending on the type of induced pathogen. Recent research has shown that CSF NLR is a more effective diagnostic technique for differentiating between bacterial and viral meningitis in children [13].

Results and Discussion

Corticosteroids, such as corticoid, may be used. Early corticoid treatment improves the outcome in individuals with acute bacterial infectious illness while reducing the risk of duct trauma. Further different antibiotics such as Penicillin G, Macrolides, Carbapenems, Vancomycin and many more are used in treatment of bacterial meningitis and are summarised in Table 1 [14].

TABLE 1: Different antibiotics used as therapeutics in bacterial meningitis.

Bacteria that causes meningitis	Mainly infected age groups	Antibiotics
<i>Streptococcus pneumoniae</i>	Children<5 years; Adults>50 years	Penicillin; Macrolides
<i>Neisseriameningitis</i>	Children<5 years Adolescents	Penicillin, ceftriaxone, ciprofloxacin, rifampicin
Group B <i>Streptococcus</i>	<3 months	Penicillin G, clindamycin, erythromycin, fluoroquinolones, ampicillin, first-, second-, and third-generation cephalosporins, carbapenems, vancomycin
<i>Streptococcus suis</i>	Adults	Penicillin G, ceftiofur, amoxicillin, gentamicin, florfenicol, fluoroquinolones
<i>Escherichia coli</i> K1	<3 months	Gentamicin, ceftriaxone, penicillin g, ampicillin, amoxicilline, meropenem

Because bacterial meningitis will not be completely eradicated by vaccination, additional interventions will be required to limit fatality and its consequences. Meningococcal vaccinations provide protection against meningococcal disease in order to protect autistic kids, teenagers, and adults from epidemics or other high-risk conditions, polysaccharide vaccinations are available

(military recruits, university students, travelers). It's also possible to use it in conjunction with antibiotics. In a study it was revealed that Nanoparticles are also useful for the diagnosis and treatment of brain illnesses like bacterial meningitis and might be seen as reviving promising systems for targeted drug delivery CNS [15].

Role of bioactive components

As a substitute to mock pharmaceuticals, numerous of phytochemical and pharmacological plants, herbs, as well as spices have been advocated as a considerable cause of natural biocides to treat bacterial infections (Table 2). Essential oils originating from medicinal plants have been used for this purpose frequently based on the concentration of bioactive compounds in them. Flavourings have been demonstrated to be functional in the infections therapy present in urinary tract, respiratory tract, and a variety of other ailments. In a study published in 2021 discovered that bioactive components in tea tree essential oil have antibacterial action against *E. coli*, *S. Typhi*, and *C. koseri* [16].

TABLE 2: Different bioactive compounds along with their sources and targeted microorganism.

Type of bioactive compound	Source	Targeted microorganisms
Flavonoids	Citrus plants	<i>E. coli</i> , <i>V. harveyi</i>
	<i>Terminalia bellirica</i> fruits	<i>C. albicans</i>
	Green tea	<i>P. gingivalis</i>
	Apple	<i>E. coli</i>
Alkaloids	<i>Terminalia chebula</i>	<i>P. aeruginosa</i> , <i>E. coli</i> , <i>S. aureus</i> , <i>A. tumeficiens</i> , <i>B. subtilis</i>
Terpenoids and essential oils	<i>Nigella sativa</i>	<i>S. aureus</i> , <i>L. monocytogenes</i>
	Cotton seeds	<i>P. vulgaris</i> , <i>E. coli</i> , <i>P. aeruginosa</i> , <i>S. epidermidis</i> , <i>B. subtilis</i> , <i>B. cereus</i>
Lectins	<i>Solieria filiformis</i>	<i>P. aeruginosa</i>
	<i>B. triquetrum</i>	<i>Streptococcus spp</i>
α -pinene, limonene and γ -terpinene	Tea tree	<i>E. coli</i> , <i>S. Typhi</i> , and <i>C. koseri</i> .

Garlic's main element, allicin, has been demonstrated to be useful against a variety of ailments, including meningitis. Garlic's allicin and other chemical compounds are high in antioxidants that have antiviral and therapeutic medication properties. Reishi mushrooms include triterpenes and polysaccharides, which help to strengthen immune system and reduce inflammation produced by the disease [17]. According to Organic Facts, the chlorophyll that is commonly associated with the process of chemical change in plants really has a structure similar to haemoprotein. As a result, red vegetative cell synthesis improves, resulting in increased natural action, blood purification, and faster recovery and repair of infectious illness damage. Olive Leaf Extracts will be used as a natural treatment for infectious disease in the form of dried, liquid, or capsules. Hyperforin has the capacity to transmit through both the blood-brain and Blood-Testis Barriers (BTB), making it a potentially useful medical medication against infectious disease [18]. Ginseng's active compounds, known as ginsenosides, are thought to work directly on the infected membranes, eliminating the infection and hastening the recovery process of infectious disease. Ginseng can be eaten directly or stewed in a tea to reap the benefits of this ancient treatment in restoring your health [19].

Urtica dioica L, sometimes acknowledged as vicious nettle, is a significant curative herb which has been used since primeval times. It's an Urticaceae family herbaceous perennial blooming plant. Antibacterial, antifungal, antiviral, and antioxidative properties are all present in this plant. Furthermore, in static circumstances, stinging plant leaves crude extract has been used to reduce inflammation and manage hyperglycemia. AgNPs derived from UD extract are often used to rescue cirrhotic rats' livers. AgNPs made from *Urtica urens* are an effectual nematicide adjacent to *Meloidogyne*, a root-knot nematode. The antioxidant and antibacterial activities of UD-AgNP aqueous and methanol extracts reveal a numeral factors, inculcating the amount of AgNO₃ present. AgNPs in combination with antibiotics have a stronger antibacterial impact than AgNPs unaccompanied, and hence can be employed in the healing of bacterial infections [20].

Conclusion

Considering breakthroughs in identification as well as therapeutics, bacterial meningitis is still one among the most popular as well as deadliest infections on the planet. The most important factors in minimising morbidity and death in individuals with symptoms suggestive bacterial meningitis are illness prevention and early start of appropriate therapy. The microorganism

extracted, the patient's age and comorbidities, and the severity of the presenting sickness all have an impact on the prognosis in this condition. Various studies for the treatment of this disease are designed to detect a relevant clinical outcome by using various antibiotics and vaccines. Moreover, apart from these treatments, the bioactive components are also playing a significant role in treatment of various diseases as confirmed by various studies. The role of bioactive components can be further explored for bacterial meningitis on the basis of previously published reports. Various bioactive components such as flavonoids, polyphenols, tannins, saponins help in attenuating various neuronal diseases.

Furthermore, there is necessity to test the plant derived components for different pathways of bacterial meningitis. New and more specific treatments via using different bioactive components taken from different plants extracts should be studied and implemented for the future perspective. These bioactive components might have some inhibitory mechanism against the invading bacteria and these mechanisms are need to be studied via using different plants in the treatment of various bacterial diseases including bacterial meningitis. Various studies confirmed that silver nanoparticles also possess the antibacterial property, these AgNP's should be used along with plants extracts that possess antibacterial, antifungal, antiviral and also antioxidant properties, so that the emerging diseases can be cured more effectively and efficiently.

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