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A Review on Antimicrobial Activity of Silymarin

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Abstract: ***Silymarin and its flavonolignan isomers, silybin, isosilybin, dehydrosilybin, silychristin, silydianin, and a few flavonoids mainly taxifolin, have been subjected to a variety of antimicrobial investigations due to extensive traditional uses and low side effects. Antimicrobial activities for silymarin and active seed extracts of Silybum marianum against different bacteria, fungi, viruses and parasites have been reported in recent years. The sound results for antimicrobial effect of silymarin make it a good candidate to synergeticly enhance the inhibitory activity of existing antimicrobial agents. Moreover, different studies have been done to increase the antimicrobial activity of silymarin, including synthesis of different chemical derivatives to increase its water solubility as well as synthesis of silymarin-loaded nanoliposomes to increase its antimicrobial activity. This review aims to summarize previous antimicrobial studies of silymarin in regard to its application in the future studies as an alternative natural antimicrobial agent.***

Keywords: silymarin，antimicrobial agent，silybin，bacteria, fungi, viruses

1. Introduction

Silybum marianum, commonly known as milk thistle, is an ancient medicinal plant which has been used from ancient times as herbal extract for treatment of different diseases such as liver and gallbladder disorders. The plant widely spread in Mediterranean region notably in Algeria [1].

Nowadays, it has been preferred as an alternative medicine in some countries [2]. Milk thistle is available as a dietary supplement in the USA. It is prescribed in Europe for its safety and well tolerance [3-5].

The active constituents of milk thistle are obtained from its dried seeds. The seeds contain approximately 70 to 80 % silymarin and 20 to 30 % chemically undefined fraction composed of polymeric and oxidized polyphenolic compounds [6]. Silymarin is a mixture of flavonolignan isomers: silybin, isosilybin, dehydrosilybin, silychristin, silydianin, and a few flavonoids mainly taxifolin [7]. Silymarin exhibits a wide spectrum of biological and pharmacological activities, which includes anti-oxidative, anti-inflammatory, anti-carcinogenic, anti-metastatic, anti-fibrotic and anti-angiogenic effects and its activity against lipid peroxidation and its ability to stimulate liver regeneration [8]. Silymarin can also inhibit some well-known hepatotrop viruses [9]. Its antiviral effectiveness against hepatitis B and especially hepatitis C viruses is well defined [10, 11].

Recently, silymarin has been reported to show antimicrobial activities against various microbe.

2. Antibacterial and antifungal activity

Bacterial infection is one of the most important infectious diseases. Hence, the researchers have been launched for achieving new antibacterial drugs isolated from different sources in more than 50 years of study. Despite the development and progress of antimicrobial agents, there are still special needs to find new antibacterial agents due to development of drug-resistant bacteria[12]. Oliveira *et al*. investigated the antibacterial and antifungal activity of silymarin and its major constituent (silibinin) against different multiresistant microbial bacterial strains from the clinical isolates. Silymarin demonstrated antimicrobial activity of little significance against the bacterial strains tested. While , Silymarin and silibinin appear to show synergistic properties when combined with antibacterial drugs[13]. Jung *et al*. also found that silybin showed a remarkable synergistic activity in combination with some antibacterial agents against drug-resistant bacteria. Therefore, silybin has a potential as a combination therapeutic agent against multidrug-resistant bacteria[14]. Kang *et al*. also had a similar conclusion. they found that silibinin combination with oxacillin or ampicillin exerted synergistic effects against clinical isolates of Methicillin-resistant *Staphylococcus* aureus [15].

Lee *et al*. reported the synergistic combination effects of silibinin with antibiotics against tested oral bacteria, whereas, their results suggest that silibinin combined with other antibiotics may be microbiologically beneficial and not antagonistic[16]. Evren and Yurtcu also demonstrated that silymarin shows antibacterial and antiadherent/antibiofilm activity against certain standard bacterial strains which may be beneficial when used as a dietary supplement or a drug[6]. Pereira *et al*. have found that silymarin is potent in neutralising the clinical isolates of multiresistant bacteria [17]. Jahanian *et al*.investigated the effect of dietary supplementation of silymarin in broiler chicks. And their results indicate that silymarin could improve performance by suppressing ileal bacteria and enhancing absorptive surface area in aflatoxin-challenged broiler chicks[18].

Lee *et al*. found that Silybin has a potent antibacterial activity, more potent than silymarin, against gram-positive bacteria, whereas it demonstrated antimicrobial activity of little significance against gram-negative bacteria or fungi. The main reason is that silybin inhibited RNA and protein synthesis on gram-positive bacteria[19].

3. Antiviral Activity

With the evolution of viral disease, many of them develop resistance to existing pharmaceuticals. Hence, the increasing requirement for antiviral substances will be more highlighted. Plants , which is a rich source of phytochemicals, provides novel leads against viral diseases[12]. It has been demonstrated that silymarin as a plant derivative has a wide range of antiviral activity against different viruses. It has been demonstrated that silymarin has a range of antiviral activity against different viruses.

McClure *et al*. found that silymarin block hepatitis C virus (HCV) infection and inhibit T cell proliferation in vitro. Silibinin, a major component of silymarin, inhibits T-cell proliferation and HIV-1 infection[20]; Moltó *et al*. found that coadministration of silymarin with darunavir-ritonavir (a kind of anti-aids drugs)seems to be safe in HIV-infected patients[21].Song *et al*. reported silymarin efficacy against influenza A virus replication. These have been shown to be toxic to influenza A virus and not to normal cells. Therefore, the potential of silymarin working on influenza virus infection merits greater attention[22].Wang *et al*. evaluated silibinin's activity against S. *aureus* alpha-toxin secretion. In addition, silymarin provides effective protection on the lung injury of staphylococcal pneumonia[23].

4. Enhancing the Bioavailability and Solubility of silymarin to Improve Antimicrobial Activities

The optimum potential of silymarin is limited because of poor oral bioavailability and insufficient solubility in aqueous solvents leading to poor absorption, fast metabolism, and quick systemic elimination. For overcoming this obstacle, nanocarriers like silymarin-loaded PLGA (poly lactide-co-glycolide) and silymarin nanoparticle formulation were investigated and their better bioactivity and bioavailabilityas well as increased cellular uptake compared to silymarin were reported. Yang. *et al*. develop a novel silymarin-loaded solid nanoparticle system with enhanced oral bioavailability[24]. Yang *et al*. develop a procedure to improve the dissolution and bioavailability of silymarin (SM) by using bile salt-containing liposomes that were prepared by supercritical fluid technology (ie, solution-enhanced dispersion by supercritical fluids [SEDS]). Their results illustrate that liposomes containing a bile salt can be used to enhance the oral bioavailability of SM[25].

5. Conclusion

Silymarin has been found to possess many biological properties, including extensive *in vitro* antimicrobial activity. Among all former studies on antimicrobial activity of silymarin, the promising effects are against mostly bacteria, fungi and viruses, at least for using the silymarin as a complementary compound in combination with other existing medicines to enhance the inhibitory activity. With respect to the studies on antibacterial activities of silymarin, the promising results are against mostly *Staphylococcus aureus* and *Escherichia coli*, although silymarin revealed bacteriostatic and bactericidal effect against various bacteria [1]. Regarding the studies on antifungal activities of silymarin, the most significant effect was found against *Candida* species[13]. The extensive antiviral effects of silymarin against sensitive hepatitis C or B virus nominate this compound as a useful drug for the treatment of chronic liver diseases [8, 26, 27]. Treatment options are limited in infectious diseases caused by resistant or multidrug-resistant microorganisms. This has created the need to search new approaches. Using silymarin or its derivatives as antimicrbial compounds indicate the research direction. In spite of various antimicrobial activities of silymarin, no real clinical uses have been reported for this compound in this regard, demonstrating the need to extend the study of their therapeutic use.

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