

Review Article



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METAL ION CONTAINING ANTI-BACTERIAL GEL: AN OVERVIEW

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Abstract

The antibacterial properties of metal ions like copper and zinc sulphate have been investigated for skin infections occur commonly and often present therapeutic challenges to researchers due to the growing concerns regarding multidrug-resistant bacterial, viral, and fungal strains. However, the synergistic activity between these two metal ions as antimicrobial ingredients has not been evaluated in topical formulations. Formulation of the gels and creams was followed by evaluating their organoleptic characteristics, physicochemical properties, and *in vitro* antibacterial activity against *Escherichia coli* and *Staphylococcus aureus*. Zinc sulfate and copper sulfate had a strong synergistic antibacterial activity in the creams and gels. In this paper evaluated and confirmed the synergistic *in vitro* antibacterial effect of copper sulfate and zinc sulfate in a cream and gels.

Keywords: Metal Ions, Antibacterial Gels, Copper Sulfate, zinc sulfate.

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Introduction

The skin infections normally occur and available therapeutic challenges to research's, despite the numerous existing many antimicrobial agents available today. The necessity for developing new antimicrobial means has increased significantly due to growing concerns regarding multidrug-resistant bacterial, viral, and fungal strains. Consequently, attention has been devoted to safe, new, and/or alternative antimicrobial materials in the field of antimicrobial chemotherapy. It is one of the most common dermatological conditions encountered in babies while using diapers and is estimated to occur in up to 35% of babies between the ages of 9 and 12 months [1-6]. Its development is multifactorial, including skin wetness, friction, skin irritants, and pH change, which favors the growth of microorganisms including *Candida*, *Staphylococcus*, and *Streptococcus*. It has been shown that zinc and copper ions have antimicrobial activity against *Staphylococcus aureus* and *Candida albicans*. Studies have shown that zinc and copper salts exhibit inactivation of HSV both *in vivo* and *in vitro* [7-13]. Zinc sulfate was found to have an antimicrobial effect in

treating cold sores. The molecular mechanism of its therapeutic effect was found to be the drastic inactivation of free virus in skin tissues, intercellular vesicles, and blisters. Pityriasis versicolor is a superficial fungal infection of the skin, usually caused by *Malassezia* species. It is one of the most common skin diseases in tropical and subtropical areas and is characterized by fine scaly patches and macules. The zinc sulfate and copper sulfate shown the strong effective in this disease [14-18].

In recent years, a number of metal ions have been studied as potential antimicrobial agents, including silver, copper, zinc, iron, magnesium, and titanium. Zinc, alone or as an adjuvant, has been found to be advantageous in a number of dermatological infections and inflammatory diseases owing to its modulating actions on macrophage and neutrophil functions, natural killer cell/phagocytic activity, and various inflammatory cytokines. Zinc sulfate has been studied *in vivo* in a number of diseases, including warts, herpes genitalis, pityriasis versicolor, and acne vulgaris in varying concentrations. Copper is well known for its antimicrobial properties. It has been used as an algicide, germicide, and fungicide for decades. Several antimicrobial mechanisms of copper were proposed in recent articles, including reactive hydroxyl radical formation leading to damaged cell integrity, denaturation of DNA by binding of copper to protein molecules, and inactivation of enzymes and obstruction of functional groups of proteins from displacement of essential ions. Additionally, topically applied copper sulfate and

hypericum perforatum were found to be efficacious *in vivo* in the treatment of herpes skin lesions [19-30].

Even trace amounts of metal ions are able to catalyze oxidation reactions in fatty compounds in products, leading to deterioration including odor formation, color change, and physical and/or chemical instability. Metal ion reactions with the ingredients in the formulations can affect the quality, efficacy, consumer appeal, and shelf-life of formulations. Stability of product and of the antibacterial activity was studied for 12 weeks at two different temperatures in two different containers [31].

GEL

Topical gels are semi solid homogenous preparation used to cure and treat topical diseases. Gels are more hydrophilic in nature so the rate of released drug or active ingredient was fast. A gel consist of two component, three dimensional cross linked material which contain proportionally large amount of liquid medium to form adequate rigid network which immobilized the liquid continuous phase. Inorganic particles and organic macromolecules both are used to form a structural network of gel. In chemical gel the particles are associated with permanent covalent bonding while physical topical gels are associated by weaker and reversible secondary intermolecular forces like hydrogen bonding, electrostatic interactions, and hydrophobic interaction and Vander Waals forces [32]



Fig01: Gel

General Mechanism of Antibacterial-Metal Activity

Metal ions or metal ion binding components play important roles in biological processes, and their rational design could be used to develop new therapeutic drugs or diagnostic probes. Normally all Metal ions exhibit wide range of chemical and physical properties that define their mechanism of cell toxicity. They can exist as many different chemical species depending on factors such as pH, ionic strength, temperature, binding partners and the reduction potential of the local environment. Such as the cytoplasm is a strong reducing environment, especially compared to the periplasm of Gram-negative bacteria. This significantly affects the oxidation state of metals and thus metal speciation. Additionally, metals are typically not freely available inside cells. Instead, a complex network of transporters, metalloregulatory sensors and metallochaperones regulate metal speciation and availability, and ensure the directed transport to e.g.

metalloproteinase, including metal-dependent enzymes, structural proteins and metal storage proteins which serve as biological reserve. In general, metal speciation strongly influences its bioavailability and reactivity, and thus represents an important physicochemical property for metal toxicity [33].

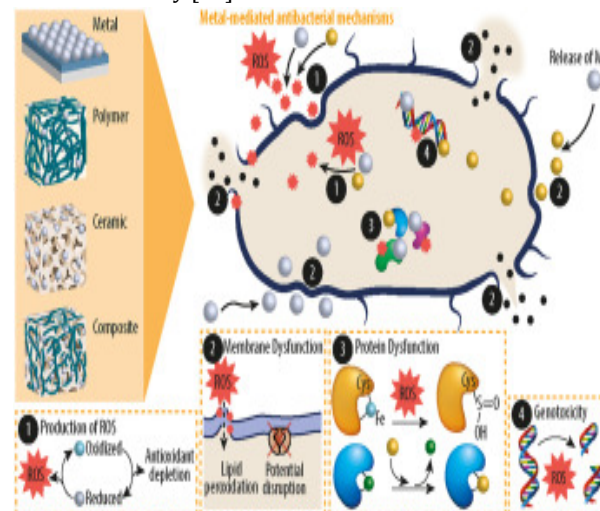


Fig 02: Metal Complex with Antibacterial agents

Advantages of Gel Formulations

the gel has several key benefits over conventional semisolid dose formulations [34]

1. Compared to other formulations, gels are simple to manufacture.
2. Gel is a sophisticated, non-greasy composition.
3. Gels offer fantastic adhesion to the application region.
4. Gels are eco-friendly and biocompatible.
5. be incredibly resilient to stressful situations.

Disadvantages of gel formulation

Despite having a number of benefits. Gel formulations can come with certain drawbacks [35, 36].

1. Gels have a more gradual and persistent effect.
2. The additives or gelators could irritate people.
3. The risk of microbial or fungal assault on gel is increased by the presence of water.
4. The formulation's solvent loss dries to gel.
5. In some gels, flocculation results in an unstable gel.

Ideal Properties of Topical Gel

- The gel should be clear and homogenous.
- The gel should be easily broken when shear or force is applied during shaking the container.
- The gel should be inert in nature.
- The gel should be not sticky.
- The gel should be never interacting with other formulation component.
- The gel should be stable.
- It should not be irate the skin or any part where the gel is applied.
- It should have anti- microbial activity [37, 38].

Formulation of Gel

All the ingredients were collected as per the required amount to formulate the 50g gel preparation. For this, mixing of the formulation ingredients was done in two

different beakers. Water was divided equally in two beakers, in the first beaker the required amount of metal ions (Zinc and copper sulfate) was added and dissolved, to its Page 5/13 calculated amount of propylene glycol 400 was added and in another beaker, Carbopol 940 was added and dissolved and to it EDTA and methyl paraben were added and dissolved. After that both the solutions in the beaker were mixed in a single beaker and at last triethanolamine was added drop by drop to obtain the consistency of the prepared formulation [39, 40].

Method for Preparation of Gel

There are 3 methods for preparation of gels.

1. Fusion method

In this method the vehicles, gelling agents, additives and drug are blended at high temperature to until a semi solid texture was not formed.

2. Cold method

In this method all the component exclude drug or active pharmaceutical ingredient is heated and blended simultaneously and then lower the temperature of formulation, then add drug and again blending was started until the gel was not formed.

3. Dispersion method

In this method the gelling agent is stirred with water until the gelling agent is swell up and then drug is dissolved in medium and incorporated into it. Add buffer solution to adjust the pH of the gel if necessary [41-43].

Gelling Agent

Gelling agents are the polymers that are used to structural network or provide texture to the gels. Gelling agents are classified as follows:-

Natural: - Gelatin, Xanthine, Cassia Tora, collagen, pectin and Guar gum etc.

Synthetic: -Carbopol 934, Carbopol 940, Polaxamers and Polyvinyl Alcohol etc.

Semi synthetic: -Hydroxypropyl methyl cellulose, Carboxyl methyl Cellulose and Hydroxyethyl Cellulose.

Additives Used in Gel Formulation

Preservative

Preservatives are used to make the gel long lasting and prevent them to spoil .E.g., Methyl Paraben and Propyl Paraben etc.

Drug solubilizer

Drug solubilizer is used in the case of drug having poor solubility. Some drugs are poorly soluble in medium so drug solubilizer helps to dissolve the drug in the medium. E.g., Triethyl-o-amine and PVP (Polyvinylpyrrolidone) etc.

Stabilizers

Some gels containing heavy metals and agents which is stabilized by chelating agent, such as E.D.T.A. (Ethylene diamine tetra acetic acid) [44, 46].

Evaluation Parameters of Topical Gel

- 1) Appearance and homogeneity
- 2) Spreadability
- 3) Extradurability
- 4) Stability Studies
- 5) Viscosity

6) Diffusion studies

7) Drug Content

Conclusion

In this review, antibacterial gels were study with copper and zinc sulfate, which act as strong antibacterial agents. During this study, the quality, appearance, and stability of many gels exhibit were affected by the highly reactive metal ions. A major finding of this study is that copper sulfate and zinc sulfate have a synergistic antibacterial activity in gels. In this review article, we focused our attention on the most prominent metal-based complexes developed in the last couple of years for their antibacterial applications.

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Author Contribution

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