ABSTRACT
In this review we have focused upon the various wound types, wound dressing stages, and wound dressing classification and characteristics. The main objective of this review is to explain the purpose of wound dressings and different types of wound dressings used. Further we have emphasized upon various biomaterials employed in dressings and their need in specific wound dressings. Biomaterials are used in the dressings to improve the healing rate of the injury, maintain moisture at the area of wound, hemostasis and reduce inflammation. So, to achieve this purpose, various approaches of wound dressings and the role of various biomaterials are also discussed. The properties, methods of preparation, advantages, and disadvantages along with future scope are discussed.

Keywords: Skin, Wound, Healing, Biomaterials, Dressing.

INTRODUCTION
Wound dressing is used to protect the wound from external environment, invading microbes, provides support in order to prevent further damage of the wound and allows faster healing of the wound by providing favourable conditions for the healing of the wound. To understand the healing action of the wound dressings, it is essential to know about the skin, wound and the healing stages of the wound.

Skin
Epidermis and Dermis are the two major layers of the skin (Figure 1). Most of the wounds are caused due to the disruption of these two layers.

Epidermis
The epidermis consists of five layers:

- **The Stratum basalis** Stratum basalis is the deepest and most closely associated with the dermis. It is made up of melanocytes, keratinocytes, and stem cells.¹

- **The Stratum spinosum layer** It comprises of many layers of cells connected with the help of desmosomes, which permits the cells to stay closely connected to one another and look like spines.²

- **The Stratum granulosum** This consists of multiple cell layers with granules rich in lipids. As the cells get away from the nutrients present in the deeper tissue, they begin to immortalize and their nuclei disappear.²

- **The Stratum lucidum** This is only found on the soles as well as palms' thick skin and is composed of mostly immortalized cells having nuclei.¹

- **The Stratum corneum (Keratin layer)** Stratum corneum is the epidermis' topmost layer. The cells are flat, and the filaments of keratin have lined up to form macro fibres with disulfide cross linking.¹

Dermis
The dermis is a tough and resilient layer with specialised structures and protects the body from mechanical injury.¹ The uppermost thin layer of the dermis is called papillary dermis Reticular dermis layer is deeper than this. The layer which is thick in the connective tissue known as the dermis gives strength and flexibility to the skin. It is made of collagen as well as elastin.¹ The top layer of the dermis is papillary dermis that usually forms papillae by folding which extends into the epidermis like tiny finger-like projections, while the lower layer of the dermis is reticular dermis.²
Wound
“A wound is a break in the continuity of the epithelial lining of the skin or mucosa caused by physical or thermal trauma”. World Health Organization (WHO) 2016 says that around 265,000 deaths are occurring every year due to burns and many deaths are occurring due to acute as well as chronic wounds. Acute wounds and chronic wounds are the two types of wounds. Acute wound is an injury that occurs to the skin unexpectedly because of an accident or surgery. An acute wound always heals in an anticipated duration, typically eight to twelve weeks according to the dimensions, depth, and also the range of injury in the layers of dermis including epidermis. The acute wound healing process includes cell division, the synthesis of new extra cellular matrix, chemotaxis, neovascularization and the scar tissue formation and remodeling. Wound Fluid of acute wounds aids in healing of the wounds by providing the supplements necessary for the cell metabolism, helps tissue repair cells migrate to areas of need, such as dead or injured tissue. It promotes a process known as auto lysis that separates it from the tissue it was attached to the healthy tissues. Chronic wounds do not heal in their expected stages and cannot be repaired in a timely and orderly fashion. They include venous leg ulcers and pressure sores. Some wounds do not heal properly or in a timely fashion, which results in non-healing chronic wounds. When compared to acute wound exudates, the constituents of chronic wound exudates vary significantly. Chronic wound’s exudate production may be continuous as a result of ongoing inflammation. Venous ulcers, arterial ulcers, diabetic foot ulcers, Pressure ulcers are some of the types of chronic wounds.

Exudates
In response to local inflammation, exudates comprises of fluid as well as white blood cells that migrates to the site of injury from the circulatory system. This response results in enhanced permeability, which results in increased production of exudates. There are different types of exudates and they are serous, sanguineous, serosanguineous and purulent (Figure 2).

The Wound Healing Process
Every body tissue has the ability to heal through either of the two mechanisms: regeneration or repair. “Regeneration, which is more limited than repair, is the replacement of damaged tissues by identical cells”. In humans, a few cells, such as epithelial, liver, and nerve cells, regenerate completely. Repair is only the primary mechanism of healing in which the tissue which is damaged is replaced by connective tissue, which forms a scar. Wound healing is the physiology of the body’s replacement and restoration of function to damaged tissues. The following are the four steps of wound healing process

1. Vascular Response
Any injury to the skin that pierces the dermis causes blood loss. To prevent blood loss, the ends of the blood vessels which are damaged constricts very soon. The exposure of blood to air aids in the initiation of the process of clotting of the blood, which is accelerated by aggregation of the platelets. The coagulation cascade is a complicated chain reaction that results in the formation of a blood clot.

2. Inflammatory Response
The initial inflammatory response entails cell recruitment to combat potential wound bacterial contamination as well as the cytokine secretion stimulation to stimulate dermal and epidermal processes. If inflammation exceeds a certain level, it impairs healing, stop the healing process and destroy the early migratory effect.

3. Proliferation
The first manifestation of the early matrix is extensive fibroblast proliferation, which occurs following the suppression of the first inflammatory reaction. This vast proliferation is associated with formation of early granulation-tissue, as opposed to mature granulation tissue associated with collagen fibres deposition at the end of the wound-healing process. Mature granulation indicates an advanced phase of healing and is visible after the epidermis has completely formed, granular differentiation has started, and fibroblast proliferation has been suppressed.

4. Maturation/Remodeling
After three weeks, the injured skin again gains its strength as well as elasticity and collagen and elastic fibres undergo reorganisation for last dermal reconstruction because of the fibrocyte realignmen. If all these stages are compromised, then there is a delay in the wound healing.

Different wound dressings act on various stages of the injury concerning the type of biomaterials used. These wound dressings have different characteristics as discussed below.
Characteristics of Wound Dressing

- Thermal insulation and gas exchange should be possible with the wound dressing.\textsuperscript{14}
- The wound should be kept moist at all times.
- It should be biocompatible, biodegradable with no cytotoxicity and antigenic or inflammatory stimulation is absent. Porosity and morphology are important for accelerating and improving wound healing because they ensure water and gas permeability as well as the capability to keep the wound bed moist.\textsuperscript{15}
- It should also prevent secondary infections and be simple to remove without causing trauma.\textsuperscript{15}

There are several types of dressings for the wound (Table 1) and every type of dressing is used for specific purpose. These Wound dressings are made in different approaches based on the necessity of the wound. Some of the types of wound dressings are discussed along with their properties, functions, methods of preparation, analysis, advantages and disadvantages.

Approaches for Developing Wound Sressings

Films

Transparent, long-lasting, conformable, easy to work with, adhesive, low-cost, semi-permeable to oxygen and water vapor but impermeable to bacterial contamination liquid. As alginates have good film forming properties, they are mostly used in the preparation of films, particularly alginate composite films like CS/HA composite films. These films are mostly prepared by casting method. Hitatang Xu conducted a research on Vaseline gauzes healing rate and CS/HA film composite and it was found that the CS/HA film composite have shown greater healing than Vaseline coated gauzes in the animal tests. In DFU treatment, minor burns and donor sites film dressings have also been developed and used. A major drawback of these type film dressings is that they should only be used on low-exuding wounds such as protective dressing for external pressure ulcers as well as in applications lasting 4-5 days prior to the replacement.\textsuperscript{16,17}

Hydrogels

Hydrogels are semi-solid gels having 3D structures derived from hydrophilic polymers. They have greater permeability, good biocompatibility and also the ability to maintain optimum moisture at the wound site. They are formed by the physical cross linking like ionic interactions, hydrophobic interactions and hydrogen bonding; and chemical cross linking like conjugation, free radical polymerization, and enzymatic reactions. Hydrogel dressings are composed of hydrophilic hydrogels such as poly (vinyl pyrrolidine) and poly (vinyl acetate) (metacrylates). They are sometimes used in conjunction with alginates because they can create films by combining the properties of gel with the elasticity of alginate. Because hydrogels are 70-90% water, they cannot absorb large amounts of exudates.\textsuperscript{18,19} Dry chronic wounds, pressure ulcers, necrotic wounds and second degree burn wounds are all treated with hydrogels (Table 2).\textsuperscript{20}

Disadvantages

Used only in or wounds with little exudates production. In fact, fluid accumulation can lead to bacterial replication and infection with in the wound. Hydrogel dressings can be applied at any stage of Wound healing.\textsuperscript{28}

Sprays and Foams

These dressings are constructed from porous PU foam or polyurethane foam film with adhesive borders or without adhesive borders. Additional wound contact layers, as well as an occlusive polymeric backing layer, are included in some foam dressings to prevent the adhesion when the wound is dry.\textsuperscript{21} They are extremely absorbent, with foam attribute such as the texture, the pore size and the thickness that determine the absorbency. The open pore structure provides very high rate of moisture vapor transmission (MVTR).\textsuperscript{21} In these foam dressings, silver is the most common antimicrobial agent use. Silver foam dressings are used to prevent the infection of the wounds. As the silver has broad spectrum antibiotic activity, development of resistance for the bacteria is less and less systemic toxicity; silver compounds like silver nitrate, silver

![Figure 3: Stages of Wound healing](image)
Almost all the composite dressings consists of antibacterial substance, it may be natural or synthetic to prevent the infection in wound.

The composite dressing, in fact every dressing should be undergone some qualitative studies like dimensions, mechanical properties, dehydration rate, absorbency, WVTR, rheological studies. FTIR analysis is done to know about the chemical interactions between drug and matrix. X-ray diffraction to measure the crystallinity of the films, film expansion study and in-vitro viability assay and some other minor tests.25

Hydrocolloid as Dressing

“Hydrocolloid wound dressings are the mostly used interactive dressings. They consist of two layers: i) a colloidal layer internally and ii) an external water-impermeable layer externally. These wound dressings consist of gelling agents (CMC, Pectin, Gelatin) as well as other ingredients like adhesives and elastomers”. They are not permeable to water and because of this reason, they maintain moist environment at the wound site. They are permeable to oxygen so, the epithelialization rate and the collagen synthesis increases, reduces the P\text{t} of the exudates so, the growth of bacteria also decreases. They are applied to wounds that exudate moderate amounts of pus such asbed sores, minor burns, trauma and ulcers etc. These dressings are advised for children because they do not cause discomfort when removed.27, 20

Alginate Dressings

“Alginate bandages are made up of calcium and sodium salts containing guluronic acid and mannuronic acid moieties”. Alginate derived from algae is absorbable as well as biodegradable. Absorption is enabled by the formation of a highly hydrophilic gel that limits wound exudates and reduces bacterial contamination.20 This gel is formed by ionic cross-linking of the alginic acid solution with calcium and magnesium to form gel. Alginites are mostly used in topical applications.27

Classification of Wound Dressings

Conventional Dressings

- **Simple Dressings** A single material that serves all functions.
- **Compound Dressings** Compound dressings are made up of several materials (generally two), each one have a distinct function.28
- **Biological Dressings** Biological dressings have two major groups: 1) a human graft obtained from an alive or recently dead donor, 2) Xenograft tissue derived from animals.28
- **Synthetic dressings** This category includes all man-made materials.28

Among these dressings, biological dressings especially animal-derived organic dressings are widely used. They are also in great demand among all wound dressings.

Biological Dressing

These dressings, which are sometimes referred to as “Bioactive dressings,” are made up of biomaterials that aid in healing of

Figure 4: Composite Wound Dressing

sulfadiazine are used in the foam dressings.22 Seung Moon Lee compared some marketed foam dressings containing silver like Allevyn, Mepilex, Medifoam silver and Polymem silver. Among them Medifoam Silver has the best physicochemical properties like absorption rate, tensile strength, WVTR and antibacterial activity. Medifoil Silver has greater absorption rate because the pore size is small and the surface is uniform. Medifoam Silver and Polymem Silver have faster absorption rate than the other dressings. Mepilex Ag has very longest absorption period among all the dressings.22 Foam dressings are used in skin grafts, DFU, DVU, tracheostomy and gastrostomytubes.23

Composite

Composite dress is a two-layered wound dressing system. In fact, a composite dress is made up of an external layer which is elastic with mechanical strength that is consistent, as well as resistance to environmental effects as well as adequate supply of moisture for the wound, and an internal layer with sufficient adhesion to adhere to the surface of the wound.24 The composite wound dressings are applied on the wound with or without secondary dressings. Most composite dressings are composed of three distinct layers (Figure 4). For composite dressings, transparent film or non woven tape, adhesive borders can also be used. The wound is protected from infection by the outer layer, the middle layer is typically made of an absorbent material that moistens the area and aids in self-degrading debridement, and the bottom layer is a non-adhesive material that prevents adhesion to young granulation tissue. Composite dressings are less malleable and cost more.20 They can be woven or non-woven and are made up of either biological or synthetic materials. Composites can be prepared by two methods, they are “Fiber surface treatment and Inverted emulsion formation. Sakehai Wittaya arekul discussed on the elastic modulus, elongation and tensile strength and found that gelatin mat that is electro spun has greater elastic modulus the alginates have lower tensile strength. The composite polyglyconate mesh which is coated with PDLGA porous matrix has higher tensile strength and the percentage elongation break is greater for Electrospun poly–(L-lactide–co–ε-caprolactone). The technique named “freezedrying of inverted emulsion” is used to create porous matrix.
wound. Tissue engineering products derived from natural or synthetic tissues are also included in bioactive wound healing dressings. These technologies frequently employ polymers like, hyaluronic acid, alginites, chitosan, collagen and elastin.21

Biomaterials used in Biological Dressings

By definition, a biomaterial is “a non-drug substance suitable for inclusion in systems that augment or replace the function of bodily tissues or organs”.29

Polysaccharide Based Biomaterials

Chitosan

Chitosan is a chitin derivative naturally attained through partial deacetylation. It is an N-deacetylated derivative of chitin, but it is rarely completely deacetylated. Chitosan’s amine side group contributes to its polycationic nature as well as the formation of intermolecular complexes with carboxylic and polycarboxylic acids are well-known.30 Because of its unique biological properties, like non-toxicity and biodegradability, it has many applications in the pharmaceutical, agriculture, water treatment, cosmetics and food, alone or in combination with many natural polymers (starch, gelatin, alginates).31

Antimicrobial property of Chitosan

Chitosan has antibacterial activity only in acidic environments, which is usually assigned to chitosan’s poor solubility at greater pH. Chitosan molecules which are positively charged interact with bacterial surface residues that are negatively charged. Chitosan interacts with bacteria membranes to alter cell permeability, indicating that the mechanism of antibacterial action of chitosan derivatives was because of the cationic NH3+ group’s interaction with negative charge of the cell membranes, which enhances membrane permeability and membrane lysis (Figure 5). P31, Molecular weight, Chitosan concentration, and complex formation are all factors that influence the antimicrobial property of chitosan.32

Mechanical Property of Chitosan

The addition of MWN Ts upgrades the tensile properties of the Chitosan matrix, and as the loading of Multiwalled carbon nanotubes increases, the mechanical properties improve. Chitosan/MWN Ts nanocomposites’ mechanical properties are affected by MWN Ts loading and dispersion.33 The hydrogen bonding between chitosan and functionalized MWN Ts leads to “MWNT-chitosan solubilization” and improved mechanical performance.34

Viscosity of Chitosan

The viscosity of Chitosan from the shells of mud crab and commercially obtained Chitosan differs significantly (p<0.05). When compared to commercially obtained chitosan, the Chitosan extracted from mud crab shells had very low viscosity in 1% acetic acid solution.35

Pectin

Pectin is a major constituent of citrus byproducts and has excellent gelling properties. Pectin is a type of hydrocolloid found in terrestrial plants as opposed to seaweeds.33 Pectin is made up of poly 1-4 galacturonic acids with different degrees of carboxylic acid methylation. Pectin films are mixed with different types of polymers to upgrade their mechanical properties and thermal properties.31 Pectins having low esters forms gel by ionotropic mechanism where as the pectins forming higher esters gels when exposed to solids which are highly soluble and are having low P31.33 The films formed by pectin are appropriate for skin applications.

Starch

Starch is a desirable polymer, for many applications in wound healing as it is easily available, biocompatible, low cost biodegradable and wound healing properties. Starch has several advantages, including its widespread availability, complete compostability with no harmful substances and low cost. The majority of biopolymers on the market are made up of this renewable resource. Starch- primarily based totally biopolymers account for 85 to 90% of all to be had biopolymers. In contrast, local starch is fragile and it has terrible mechanical properties. The disadvantages of starch- based materials include low processability, high sensitivity, and long-term stability to water.36

Cellulose

Acetobacter xylinum grows in a variety of media, including coconut as well as pineapple juices, and any carbohydrate source, to produce bacterial cellulose. Microbial cellulose is an adaptable biomaterial with a distinct strong mechanical properties, nanostructure, and exceptional swelling characteristics. An inventive natural raw material for polymeric products, microbial cellulose is utilized in the fabrication of wound dressings on account of its biocompatibility, biodegradability, antimicrobial properties, hypoallergenicity and non-toxicity.37

Carrageenan

Carrageenans are hydrocolloid extracts from the seaweed class Rhodophyceae. Carrageenans, unlike alginate, are composed of multiple interconnected structures. Carrageenans are commercially available in the form of a blend of three different carrageenans. The ionotropic and cold-set mechanisms are both involved in the formation of carrageenan gel.33

Hyaluronic Acid

Hyaluronic acid is basically a glycosaminoglycan (GAG) made up of alternating units of -1,4-d- glucuronic acid and -1,3- N-acetyl-d-glucosamine joined by - (1,3) linkages. It is a
structural component of connective, epithelial and basal layer tissues from mammals, and it also functions as a lubricant and shock absorber in synovial fluid. As a result, it’s well tolerated and has no immunogenicity.  

Furthermore, due to its highly negative charge, HA has the capacity to absorb and withhold a large amount of water. On absorbing water, it swells up to thousand times of its real volume and forms a viscoelastic gel and the thickness enhances along with the molecular weight. HA promotes the healing of wound by instigating “migration, adhesion, and proliferation” of fibroblasts, keratinocytes of the skin as well as collagen synthesis.

**Alginate**
Alginate is a naturally occurring biocompatible and biodegradable polysaccharide. It is made up of a- (1-4) linked L-guluronic acid as well as b-(1-4) linked d-mannuronic acid. It consists of consecutive G and M residues as well as altering M and G residues. The physical properties and molecular weights depend upon the M and G residue sequence. The properties of calcium chloride cross-linked hydrophilic alginate hydrogels can be modified to regulate both the rate and extent of swelling, there by regulating wound exudates uptake and subsequent drug (antimicrobial) release.

**Protein Based Biomaterials**

**Collagen**
It is a plentiful protein present in the human body, and is found primarily as fibrils. Before being secreted into the extracellular space, the molecule of collagen is put together intracellularly as a procollagen molecule with a super-helix. Collagen is typically implanted in the form of a sponge with little mechanical strength or stiffness. Because of its hydrophilicity, it blends very easily with other polymers.

**Gelatin**
Gelatin is a type of collagen that has been denatured and it is produced through the collagen type I chemical, physical, or enzymatic hydrolysis. Gelatin, unlike its precursor, has the property of non-immunogenicity, biocompatibility, and biodegradability. “Type A gelatin” is produced by acid treatment and “type B gelatin” is produced by alkali-treatment. GA contains a positive charge at unbiased pH and the pI value of 8-9, while sort B gelatin (GB) incorporates a negative charge and incorporates a pI esteem of 4.8–5.4. Gelatin is commonly used as a scaffold, an absorbable compressed sponge for hemostasis and an absorbent pad for surgical use.

**Fibrin as a Biomaterial**
Fibrin is formed as the final product of the cascade of the coagulation of blood, generated when thrombin enzymatically breaks down fibrinogen. The primary function of the fibrin is to form a clot, which helps to stop bleeding and serves as the foundation for cell migration during the healing of wound. Fibrin is necessary for hemostasis and is involved in thrombosis, healing of the wound, and other biological functions as well as pathological conditions.

**Keratin**
Keratin dressings accelerate wound closure and epithelialization in chronic wounds and dermal pathologies such as epidermolysis bullosa. They also had an intriguing hemostatic effect. Finally, due to the presence of cysteine, a precursor of the glutathione pathway, keratin has an antioxidant action that is very beneficial in the context of wound healing.

**Polymers**

**PU**
Polyurethane is utilized in wound dressings owing to its semi permeable property protecting the injury from the external environment and invading bacteria. This property of semi-permeability makes the environment wet at the wound location. Its semi-penetrability makes a wet environment at the wound location, which is alluring. Adherence may be an impediment of the polymer of polyurethane that can be prevented by covering polyurethane mesh with collagen or collagen-based peptides, which significantly increments cell grip conjointly progresses tissue biocompatibility.

**Polycaprolactone**
Polycaprolactone is synthesized using auto catalyzed bulk hydrolysis and degraded linear aliphatic polyester. Polycaprolactone is non-toxic, FDA affirmed, and it is surely formed as a wide range of patterns and forms. PCL films were prepared by biaxial stretching technique. These films are very flexible as well as transparent. They have good contact with wound and also good vapor transmission. Electro spun PCL fibres are effective in treating both acute and chronic wounds. They have a fibrous structure that resembles extracellular matrix. PCL material’s poor antimicrobial properties limit its application. As a result, AgNPs are blended into the Polycaprolactone framework to guarantee the resistance to the attack of microbes. The PCL-collagen matrix functions admirably as a template, activating the integrin-l signaling pathway in order to control the development of the fibroblasts and initiate healing of the injury. Kee Woei Ng discussed on the properties of PCL films and native skin. From that we can conclude that, in PCL films very low level of fibrosis is seen and have no inflammatory reactions. The ultimate tensile strength is found to be 50-60% of the native skin.

**Applications**
Some of the biomaterials’ applications are listed below:
- Chitosan is used in various industries, like medicine, cosmetics, chemicals, metal extraction, water treatment, biochemical, and biomedical engineering.
- Regenerative medicine makes use of gelatin for Bioprinting in 3D, Culture of Stem cells, healing of wounds, Membranes that are implantable, Drug administration.
- Cellulose is used in medical applications like tissue engineering, controlled DDS, wound dressing and blood purification.
- Pectin has been used as a binder, as a transporter of drugs
in drug delivery as well as a controlled release matrix.45

• Collagen dressings are currently used to treat burns, trauma, infectious and surgical skin injuries, and chronic wounds.46

DISCUSSION

Healing of the wound is the main objective. During the process of healing, the wound undergoes many changes. For this purpose, many types of dressings are being manufactured by using various types of materials. Categorizing is necessary to control different parameters of the materials in order to get the wound healed. Among all the dressings discussed, composite dressing is versatile and can be used from mild to severely exuding wounds and foams are also used in case where absorbance is needed. The properties of materials used in the preparation of wound dressings are also discussed. Among them, chitosan, alginate and collagen are most widely used and the remaining all are used as per the requirements of the dressing. Applications of these materials in various fields are also discussed.

CONCLUSION

A biomaterial is “a non-drug substance suitable for incorporation into systems that enhance or replace the function of bodily tissues or organs”.21 The use of different biomaterials has previously been discussed; and no single biomaterial can achieve all of the desired wound dressing properties. A near-ideal wound dressing should conform to the wound site, relieve pain, promote faster wound healing, and allow patients to resume their normal daily activities.37

The treatment of wounds that are challenging to heal continues to pique the research community’s interest. The development of new components and approaches to aid in healing of persistent wounds is necessitated by a continuously expanding market, due to an increase in the number of older individuals worldwide. The market for modern wound care is currently crowded with competing technologies, the vast majority of which are polymer- and hydrogel-based dressings. Several wound dressings that are capable of delivering drugs directly to the wound bed have been developed and also been tested with preclinical models demonstrating superior efficacy when compared to their components alone. The wound dressings can be made individually or in combination as we see in composites. There may be many advances in the healing of wound with the use of many biomaterials.

Future Scope

Although there are many types of wound dressings, there is a need for the advanced technology to improve the wound healing and prevent infections and amputations. There are many technologies like Topical oxygen Wound therapy and Negative Pressure Wound therapy etc. NPWT has brought a great change in the healing of DFU. Recently, Multifunctional smart wound dressings are available where they perform a number of functions in wound healing. Other types of dressings include P61responsive wound dressings, temperature responsive wound dressings, pressure responsive wound dressings, moisture responsive wound dressings, and sustained drug release wound dressings. Even some wound dressings are using AI in treating the wound along with the biomaterials. In the near future, wound dressings consisting of biomaterials with bioactive agents will be far more effective at managing wounds.24

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