Research & Reviews: Drug Delivery

A Systematic Review on Wound Healing and Traditional Wound Care Management

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Review Article

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ABSTRACT

Burn and burn related wounds and other types of wounds pose a serious health, social and economic problems to our society. According to WHO, fire related burns cause annual deaths of more than 3,00,000 people, 95% of which occur in third world countries including India. Conventional treatments of wound involve use of silver sulphadiazine and other antimicrobial agents as ointment and cream. They are greasy in nature and stick to clothes and lack patient compliance. It is now established that effective wound healing requires moist environment.

Keywords: Wound; Chronic; Neutrophil; Cell; Silver sulphadiazine

INTRODUCTION

Wound

A wound refers to as that type of injury which damages the skin tissues and many other different body parts. Wound injury occurs by different type of reasons like during the breakage of any tissue, muscle tears, burns or a bone fracture. A wound is also originated by a surgical procedure, an infectious disease or a fundamental morbid condition. There are many types and causes of wound injury which are classified by healthcare professionals in many different ways. Usually they are classified in the two ways, one is *i.e.,* acute wounds and another is chronic wounds. The types of the wound and their causes are given in Table 1 [1].

Approximately chronic wounds infected 6 million people around the world according to the reports. According to the current estimates, about 4.5 per 1000 population infected by chronic wounds in the community while about 10.5 per 1000 population infected by acute wounds.

Thus the main objective in managing such kind of wounds is to cure the injury in the lowest period of time so as to reduce the cost and increase the patient compliance by minimizing the throb, tenderness, and blemishing to the patient. For addressing such wounds many wound dressings are available in market which satisfy one or the other properties mentioned above, this include foams, alginate dressings, hydrocolloid dressings, hydrogels etc. These dressings help in the early healing of the wounds by enhancing the growth factors, other mediators responsible for wound healing at different phases of curing [2].

Table 1. Different types of wounds and causes.

Types of wound	Causes	Healing time (Days)	CAGR 2007-2016 (%)
Surgical injuries	110.3	14	3.6
Traumatic injuries	1.6	28	1.7
Deep lacerations injuries	20.4	14	1.2
Burn injuries (outpatient)	3.4	21	1
Burn trauma injuries (medically treated)	6.5	21	1.3
Burn trauma injuries (hospitalized)	0.2	50	1.1
Pressure ulcers Injuries	8.5	-	6.9
Venous ulcers injuries	12.5	-	6.7
Diabetic ulcers injuries	13.5	-	9.3
Amputations	0.2	-	1.2
Carcinomas injuries	0.6	14	3
Melanoma injuries	0.1	14	3.2
Complicated skin cancer type injuries	0.1	28	3.1
Source: Worldwide wound prevalence by Etiology, 2009.			

LITERATURE REVIEW

Pathology of wounds

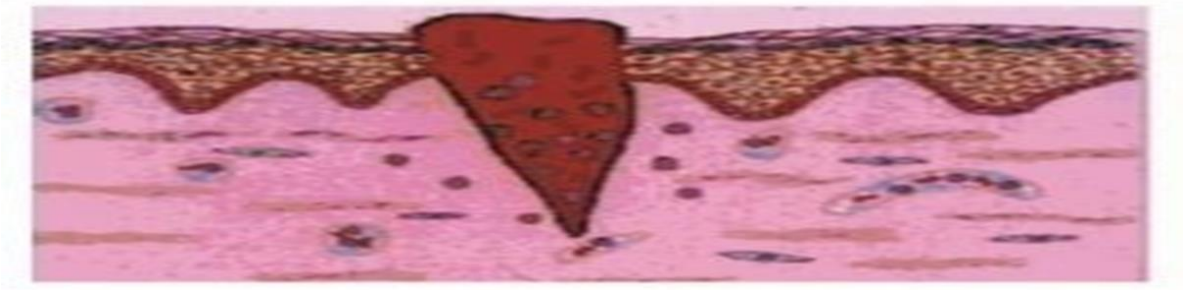
It is a very complex process to heal the wound. These have four different phases which are healing very systematically and these four phases *i.e.,* inflammatory phase, migration phase, proliferation phase and maturation phase and each phase also described by diagrams, each phase have the different pictorial presentation diagram (Figure 1) [3].

Figure 1. Different phases of wounding.

Inflammatory phase

There are of two types of sub phase *i.e.,* haemostasis and inflammation phase. They prepare the healing area and disenable the wound by causing by swelling and become excruciating, that's why activity of moving becomes cramped. This triggers the flow of neutrophils at the site of injury resulting in engulfing of debris and microorganisms by giving the first line of defence in opposition to infection. The neutrophil migration terminates after the sometime of post injury if the injury is not corrupted but if this acute inflammatory phase services, it can interfere with the late inflammatory phase. Monocytes are transferred in the tissue to macrophages in the late inflammatory phase which helps to digest and destroy bacterial pathogens, scavenge tissue debris and kill remaining neutrophils (Figure 2) [4].

Figure 2. Inflammatory phase of wound healing.



Migration

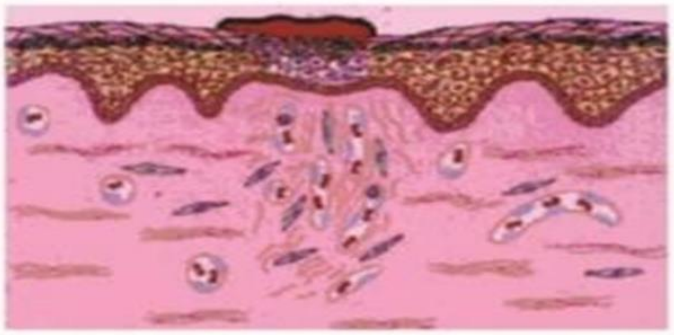
In the migration phase, replacement occurs of destroyed and damaged tissues by moving epithelial cells and fibroblasts to the wound region. These cells are growing very quickly upon the injury below the dried scab (clot) lead by epithelial thickening by revitalize (Figure 3) [5-10].

Figure 3. Migration phase of wound healing.

Proliferation

There are three sub phases *i.e.,* granulation, contraction and epithelialisation. In the proliferative phase, granulation tissue and epithelialization are made. The area of the wound identifies its duration. The migration and activation of wound fibroblasts occurs by releasing the chemotactic and growth factors from platelets and macrophages that give a variation in constitients which are important to cure injury such as glycosaminoglycans (mainly hyaluronic acid, chondroitin, dermatan and heparan) and collagen which develop an amorphous gel such as connective tissue matrix essential for cell migration (Figure 4) [11].

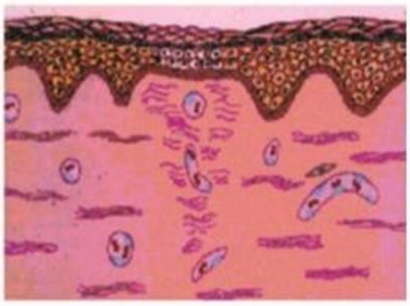
Figure 4. Proliferation phase of wound healing.



Maturation

Maturation making a well ordered lattice structure that incorporates a shakeup of new collagen fibers that gradually continual to enhance the mechanical strength of injury. The remodeling process is continual more than two years; attaining 40%-70% of the capacity of unblemished organisms at four weeks (Figure 5) [12].

Figure 5. Maturation phase of wound healing.



Wound management/wound care

From the earlier times it has been believed that the wounds heal when they are kept dry. But according to the study of George Winter, he tells that he opened many of the small partial thickness injuries on backs of the pigs to polymer film and the rest to open air. According to the George Winter, injuries healed by polymer film epithelialized two times as rapidly as the injuries exposed to air. According to the landmark study, he was says that there was an inception of a new concept of moist wound healing. According to the studies, epithelial cells are require more energy during the dry wound healing and consuming the much time and if moist wound occurs, they require lea time as comparison to dry wounds. Various other studies say that, moist wound healing can accelerate the inflammatory response and also

helps to enhance cell proliferation and wound healing in deeper dermal wounds according to the nature publishing group [13].

It has been established that the moist wound healing imitates the function of the epidermis of giving the crucial growth factors for healing. Mainly water, and the natural environment is involves in our body which makes the moist cell; so a dry cell is a dead cell. Once a cell is it prevents the flow of nutrients, other cells, growth factors etc., into the wound bed.

Benefits of moist wound healing

- Decreases desiccation and demise of the tissue.
- Angiogenesis is increased.
- Autolytic surgery is enhanced in moist wound healing.
- Re-epithelialization is increased.
- Lessen throb.

Traditional wound healing agents

In the past, these agents were used frequently and at present, these are less widely used. In the currently time, still they have some uses in certain medical settings for healing the wound injury. Topical liquid, semi-solid formulations and also traditional dressings are some examples of the traditional wound healing materials [14].

Topical dressings

Liquid formulations like emulsions, solutions and suspensions and semi-solid formulations like creams and ointments are comes under topical pharmaceutical formulations and in currently time, these are used very commonly for wound healing. Solutions such as povidoneiodine are mostly used material for wound healing at initial stage for minimize bacterial load and used to prevent the maceration of healthy cell by inhibit maceration of healthy cell by the inhibition of necrotic micro-organisms from the new developed injury. These are used as debriding and desloughing agents. Silver, povidone iodine and polyhexamethylene biguanide are some antimicrobial agents which are every so often immersed into ligatures to control or protect from infection. To removal of dead tissue, cleansing of wound is very important and for this, physiological saline solution is used. To irrigate the dry wounds, saline solution is mostly used during change the dressing to aid removal with very small or no pain. Minimum occupancy set up on the wound site is the major problem with liquid dosage forms mostly where there is a measurable degree of emanate of wound exudate. Semi-solid formulations like silver sulphadiazine cream and silver nitrate ointment is the most widely used material for inhibition of the bacterial infection on the surface of injury for longer duration of time if we compared these with solutions. Semi-solid formulations are used very rarely because these have not good rheological properties and do not absorb exudates quickly [15].

Occlusive materials

The word occlusion itself means retention of moisture. Thus, an occlusive dressing affects the wound by trapping moisture next to the wound bed thus following the principle of moist wound curing. Advancement in the science to treat wound injury, strongly favours in the use of occlusive dressings to enhance patient comfort, enhance patient compliance, minimize the risk of contamination, and minimize overall healing time. They are also termed as moist

wound dressings because they follow the conception of moist wound healing.

The characteristics of ideal moist wound dressings are:

- Retains a moist wound environment.
- Such up too much exudate.
- Removes dead space.
- Do not harm the wounds.
- Gives the thermal insulation.
- Gives the bacterial barrier.

Modern wound material

Modern wound materials are those materials in which dressings are formed for curing the wound injury. These materials are compared with the traditional wound healing materials. These have the ability to provide a moist environment at the place of wound injury. Hydrocolloids, hydrogel sheets, hydrogels, gels, films and foams etc. are comes under the modern wound healing materials [16].

Nanotechnology formulations

Nanotechnology is a speedily enlarging incorporative research based field in that both the directions of science matter and technology are united. The sizes of Nanoparticles are ranges from 1-100 nm. These nanoparticles have unique properties from their volume analogous. Nanoparticles should require different properties like physicochemical, optical and biological properties which are satisfactory to making different shaped nanoparticles according to desired applications. Silver, gold, copper and titanium elements are used for treatment since ancient times. More lately, researchers have formulated understanding of and consciousness of nanoparticles and tells about how nanoparticles can be applied for delivery of drug, diagnostic, imaging, biosensor, and for cosmetic reasons. Separate nanomaterials have been energetically explored for biological applications throughout the last few decenniums. Liposomes, dendrimers, quantum dots, fullerenes, carbon nanotubes, graphene, iron and titanium oxide, gold or silver nanoparticles are also the parts of the nanoparticles. Calcium and oxygen are NP based delivery of ions which has been used to promote angiogenesis. The distinction of ADSC to endothelial cells and angiogenesis would upgrade by the application of nanomaterial.

Nanoparticles are dissolved in the biomaterials and scaffolds to generate nanocomposite good materials that can aid wound which are healed by their antimicrobial, selective antiinflammatory and proinflammatory, and pro-angiogenic properties. Wound healing process can also affected by influencing collagen deposition and realignment. These are used in vectors for delivering gene. Intracellular gene expression and also formation of protein are changing which are associated with the wound healing process.

Wound curing either arise by primary and secondary object. In the primary object, wound edges are approximated sutured and in the secondary object wound is left open to cure *via* a bond of granulation tissue development, contraction, and reepithelialisation. The succeeding and interweaving stages of haemostasis, inflammation, proliferation, and remodeling, these all are included in the wound healing process. Haemostasis comes into vasoconstriction, where the development of a platelet plug and platelet degranulation occurs. Inflammation happens and involves in the release of pro-inflammatory factors by platelets in the first two to three days after injury, which

increase inflammatory cell proliferation and migration. The inflammatory phase is convergence by the proliferation phase and ending up to 4 weeks. Here, chemo attractants are liberate by inflammatory cells to fibroblasts, which wander into the wound to stake ground substance, type III collagen, and elastin. Angiogenesis happens concomitantly. Remodeling is that process in which rearrangement and organization of collagen fibers involves, as well as substitution of type III *via* type I collagen. It is a fine equilibrium between the inflammatory, proliferative, and remodeling phases, which results in enough wound healing.

The weighed physiologic healing process is disrupted by the systemic and local factors. Wound healing can hinder by these. Systemic factors are either congenital or acquired. A genetic disorder's range is included into the congenital factors. Faulty collagen synthesis is linked with this range of genetic disorders, raised collagen humiliation, faulty elastin synthesis, prelamin an accumulation, and raised telomere decompose. Many circumstances like diabetes mellitus, smoking, old age, deficiencies of vitamin, and treatment with antiinflammatory drugs, these all are comes under the acquired systemic factors. Infection, radiation, trauma, and poor tissue blood and neural supply, these all are the examples of local factors [17].

Owing to turmoil in the symmetry between the distinct wound healing phases, immoderate scarring following injury can generate. On the healthy skin, Keloids and hypertrophic scars are not occured. Rich vasculature, high mesenchymal cell density, and thickened epidermal cell layer are the main reasons for this. Unusually greater density of fibroblasts and unidentifiable collagen fibrils are generated by them. A protracted or immoderate inflammatory phase is credited to affect the arrival of immoderate marking. Pain, pruritis, and contractions are comes due to the keloids and also these are normally unaesthetic.

Both paucity of suitable curing and immoderate scarring endure an ordinary scrutinize and an in progress provocation for disorders analysts. The occurrence of refractory wounds is increasing as a ramification of the maturing population, developing the rectification of wound management a crucial health maintenance concept.

With woven material

Silk has been used as surgical suture material and textile fiber for many centuries. Silk has different benefits for wound healing materials, like biocompatibility, minimal inflammatory reaction, and capability for progress of wound healing, strength, firmness, light weight, and easy chemical modification. Medical research of silk in which silk is used as membrane, scaffold, and wound dressing materials. The obvious limitation of the silk is the difficulty in mass production.

Polyester/Cotton blended fabrics (P/C) are widely used in the apparel industry and decorative areas because of their complementary physical and chemical properties. P/C fabric has not only the advantages in synthetic fabric, such as high strength, good wearing resistance, high color fastness, good heat resistance and acid resistance, but also has excellent wearability of natural fabric, such as moisture absorption, breathability, and soft handle. However, P/C blended fabric shows higher flammability than any of the two components of the blend because of its "scaffolding effect" throughout combusting; hence it is hard to extinguish fire once when it starts burning, thus causing fire disaster by textile burning. But Flame Retardant (FR) textile can slow down the fire spread rate, reduce fire hazards and extend escape time, thereby protecting people's lives and property.

With conventional medicines: With silver sulfadiazine

An open wound is a crack onto the skin's surface which results in external bleeding. This also allows bacteria to move into the body, will cause infection into the body. Standard burn wound care involves prevention of infection by using topical antimicrobials (bacitracin, neomycin, polymyxin B sulfate, and silver sulfadiazine). Silver Sulfa Diazine (SSD) is used as a topical antibiotic. It is extensively useful for the treatment of burn injury diseases which is involved in second and third degree burn. Silver sulfadiazine creams or ointments are used as antimicrobial agents. But its application is touching the wounded surface is painful and may spread secondary infection. There are practical drawbacks of the medicated cream, such as, the necessity of wearing sterile gloves for its application, applying at least a 1.6 mm layer of cream, maceration after long usage, soaking to clothing, bandage and pain while applying cream on injured site etc. FDA label also recommend application of SSD topical cream 'Silvadene' under sterile conditions. These topical creams may cause few side effects like itching. Many sustained release formulations have been developed over past two decades to overcome these side effects by slowing down the release rate of formulations, like gels, emulgels, lipid based gel, sprays etc. Application of spray formulation can also decrease the chances of secondary contamination of the wound site. Spray formulation for delivery of SSD, developed aerosol formulations, where the drug is dispersed in an organic solvent acetone. Aerosol formulations require special containers. We know, gels are difficult to spray. Therefore, present formulation was aimed to develop aqueous spray formulation, which can be easily sprayed on the open wound and also reduce the possibilities of secondary infection. Aqueous spray formulations are also cheaper and less likely to produce the stinging action of hydro alcoholic sprays. Topical sprays prepared for many other drugs by different scientist also contain propellant or hydro alcoholic solvent systems.

Medicated hydrogel dressings

The hydrogel dressing which contains a medicinally active compound in it is termed as a medicated hydrogel. In the market, the hydrogels which are present, these all mostly non-medicated which suffers the wound by contamination and take a long period of time to cure wounds. Contamination and long period of time, these two are main drawbacks in the hydrogels. These two disadvantages can be overcome by use of a medicated hydrogel. During the last few years, many researchers are doing work on forming medicated hydrogels to heal the wound injury easily and for making this type of dressing; all researchers are founding the different type of materials such as synthetic origin material and normal origin material. According to the many researchers, 70% of the Ayurveda drugs have been founded from plant origin, 20% have been founded from mineral origin and the remaining 10% have been founded from animal substances. Medicated material dressings give and inexpensive drugs as comparison to traditional medicines. Traditional medicines do not give inexpensive medicine than medicated dressings. So medicated dressings have more approach than the traditional medicines. Researchers also prepared a hydrogel dressing containing honey which is well known for its wound healing activity. They were prepared and evaluated a hydrogel wound dressing containing asiaticoside a compound isolated from *Centella asiatica*.

Till date there is no hydrogel available in market which contains a medicinally active compound in it. Recently, cardiotech has announced only a FDA clearance of an antibiotic hydrogel dressing. Dr. Michael Szycher the CEO of this company stated that cardiotech is the only company in the market with a medicated hydrogel sheet product.
Thus, owing to the current availability of the hydrogel dressings and the number of advantages, there is a need of exploring the medical application of hydrogel for chronic wounds so as to improve the quality of life and loss of

income of the patients with such kind of chronic wounds [18].

RESULTS

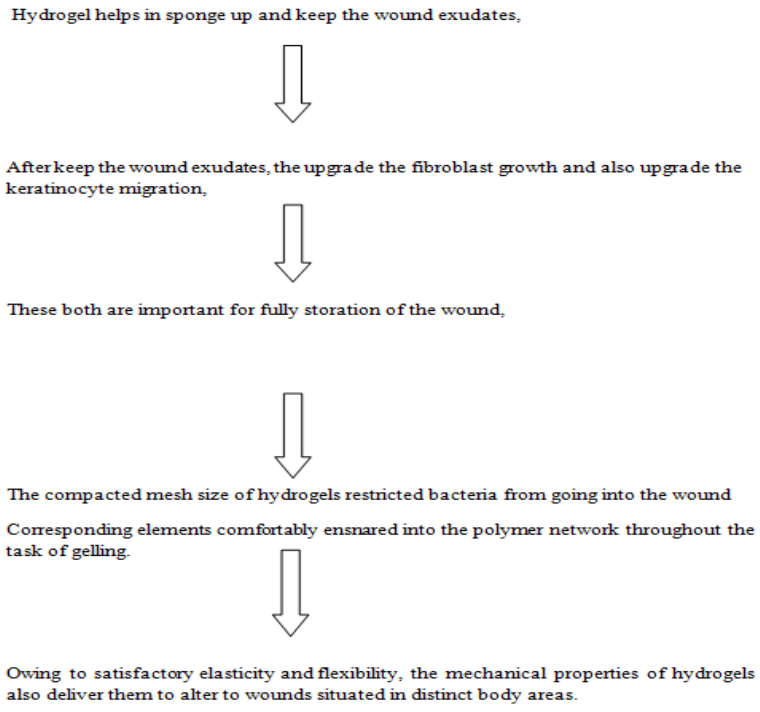
Hydrogel dressings

Different types of treatments are accessible for the treatment of limited thickness burns. All dressings are developed to soak up the wound exudates. Hydrogel dressing keeps a moist environment to make possible surgery of the gangrene and uninhibited restoration of the skin. Hydrogel dressings provide interim and give rise to wound analysis and a mechanical barrier to infections.

Hydrogels can soak up and liberation water in a capricious way according to the ecological conditions, such as ionic strength, temperature and pH. This smart behavior of hydrogels in the direction of changes of physiological variables insinuates their importance in different conditions for biomedical uses.

The internal behaviour of the hydrogels promotes skin curing process and it also used in the clinical setting since the early eighties (Figure 6).

Figure 6. This figure shows wound healing.



Hydrogels have the following properties

- Provide moist environment at the wound dressing interface.
- Possible to use on infected wounds.
- Transparent and flexible.
- Provides mechanical protection and cushioning effect.
- Should not require frequent changing.
- Comfortable and contour forming.

- Safe to use.
- Good absorption characteristics.
- Impermeable to microorganism.
- Sterile
- Available in required sizes.
- Possibility of delivering drugs without removing dressing.
- Cost effective.

Hydrogel sheet

Hydrogel sheet dressing is those dressing which create a moist wound healing environment. Moist environment is very much required for wound healing process. Hydrogel sheets absorb too much exudate. Gaseous exchanges are also occurred by these dressings and release of active drug for quick and effective cure of wound. Hydrogels sheets have antimicrobial, nontoxic and biocompatible nature. The material which is used in hydrogel sheet dressing has the functional characteristic. For the wound healing, only one material can't achieve all the conditions to recovery the wound injury that's why different type of materials are used to form hydrogel sheet.

Hydrogel sheets are prepared by different types of methods which are following

- By chemical crosslinking method.
- By radiation crosslinking method.
- By Freeze thaw crosslinking method.

DISCUSSION

Chemical crosslinking

Chemical crosslinking method is refers to those method which is used to prepare hydrogels in which chemicals are crosslinked with each other and these chemicals are like gluteraldehyde, acetaldehyde, formaldehyde and other monoaldehydes. These chemicals are utilize under the sulphuric acid, acetic acid or methanol form acetal bridges between the hydroxyl groups of PVA thus crosslinking the same. But, the main disadvantage of this method is the residues of these agents remain in the PVA hydrogels. Due to which they become toxic or rather unacceptable for use as biomedical material or pharmaceutical application. These toxic agents may influence the biological activity of the active agent being used or may degrade it. Thus, this method is usually not preferred for the crosslinking of PVA.

Radiation cross linking

It is the second method commonly employed for the preparation of hydrogels. It occurs as a result of mutual recombination of macro radicals. The radical mechanism is occurring into the radiation cross linking method which is involved owing to the radiation polymerization. These have the three steps such as initiation, propagation and termination of growing chains (PH means PVA long chain).

Activation

- $PH \longrightarrow PH^*$
- $H_2O \rightarrow HOH^*$

Free radical formation

- $PH^* \rightarrow P. + H.$
- $HOH^* \rightarrow OH. + H.$

Gas evolution

- $H. + H. \rightarrow H_2$

Energy transfer

- $PH + HOH^* \rightarrow PH^* + H_2O$

Crosslinking

- $P. + PH \rightarrow P.\text{-}PH$

Degradation

- $P.\text{-}PH \rightarrow P. + PH$

Incorporation of drug into a radiation cross linked hydrogel can be done in two ways. The drug can be either incorporated during the forming step of cross linked polymers or can be loaded into the hydrogel after the formation step as the drug may be sensitive to the gelation conditions. This method has its own advantages like

- Hydrogel formation rises by the increasing reaction and by initiation if the chemical initiators are absent.
- The overall procedure of gel development and simultaneous sterilization can be performed in single step.
- Initiation and termination of chemical reactions can be done by simply introducing or removing the material from the field of irradiation.
- The desired physical and chemical properties in the final product can be achieved by adjusting the intensity and type of radiation, irradiation time (dose) etc.

Freeze thaw crosslinking

It is the third method of crosslinking the polymer to form hydrogel. This method is mostly used method to form the hydrogel sheets. The mechanism of hydrogel formation involves physical crosslinking because of crystallite formation. This method eliminates the use of chemical cross linkers and thus addresses the toxicity issue related to the same. So, also the mechanical strength is higher of the PVA gels prepared by freezing thawing technique as compared to the chemical and irradiative techniques. This is attributed to the crystallites having a three dimensional structure. Days for freeze thaw cycling are enhances if the number and stability of these crystallites enhances and the crystallites are represented as layered structures at a molecular level and these are held with the hydroxyl groups. PVA chains helps to increase the development of crystallites and these are scattered in an unordered, amorphous polymer matrix. Many types of solvents such as dimethylformamide, ethylene glycols, Dimethylsulphoxide (DMSO) etc., are used for crystallization.

CONCLUSION

Various papers are tells that these types of solvents increase the mechanical strength which are soluble in the water. Many papers says that which solvents are soluble in water, these helps to increase the mechanical strength of dressings and also makes the PVA hydrogels transparent but these solvents should take as non-solvent for hydrogel sheets and then if hydrogels are taken for freeze cycle into freezer at -20^0C. These form the crystallites and owing to these crystallites, mechanical strength of hydrogels increases. The formation of crystallites and further the

mechanical strength of hydrogel are directly proportional to the PVA concentration, the freezing time and the thawing time. Thus, addition of a non-solvent (*i.e.,* an organic solvent) can be used to enhance the various properties of a hydrogel most importantly the tensile strength.

REFERENCES

1. Ajji Z, et al. Production of hydrogel wound dressings using gamma radiation. Nucl Instrum Methods Phys Res B. 2005;229:375-380.
2. Hassan CM, et al. Structure and applications of poly (vinyl alcohol) hydrogels produced by conventional crosslinking or by freezing/thawing methods. Biopolymers, PVA hydrogels, anionic polymerisation nanocomposites. Spinger. Newyork, USA. 2000:37-65.
3. Kumar B, et al. Ethnopharmacological approaches to wound healing exploring medicinal plants of India. J Ethnopharmacol. 200;114:103-113.
4. Madaghiele M, et al. Polymeric hydrogels for burn wound care: Advanced skin wound dressings and regenerative templates. Burns Trauma. 2014;2:153-161.
5. Mallefet P, et al. Mechanisms involved in wound healing. Biomed Sci. 2008;52:609.
6. Racovita S, et al. Polybetaines in biomedical applications. Int J Mol Sci. 2021;22:9321.
7. Naderi N, et al. Nanoparticles in wound healing; from hope to promise, from promise to routine. Front Biosci. 2018;23:1038-1059.
8. Rheinecker SB, et al. Wound management: The occlusive dressing. J Athl Train. 1995;30:143.
9. Roy N, et al. Development and characterization of novel medicated hydrogels for wound dressing. Soft Mater. 2010;8:130-148.
10. Sharman D, et al. Moist wound healing: A review of evidence, application and outcome. Diabetic Foot. 2003;6:112-120.
11. Sikareepaisan P, et al. Preparation and characterization of asiatico side loaded alginate films and their potential for use as effectual wound dressings. Carbohydr Polym. 2011;83:1457-1469.
12. Stadelmann WK, et al. Impediments to wound healing. Am J Surg. 1998;176:39-47.
13. Sulekha B, et al. Topical spray of silver sulfadiazine for wound healing. J Chem Pharm Res. 2016;8:492–498.
14. Wang T, et al. Hydrogel sheets of chitosan, honey and gelatin as burn wound dressings. Carbohydr Polym. 2012;88:75-83.
15. Yusof N, et al. Development of honey hydrogel dressing for enhanced wound healing. Radiat Phys Chem. 2007;76:1767-1770.
16. Lee WY, et al. Effectiveness of woven silk dressing materials on full skin thickness burn wounds in rat model. Maxillofac Plast Reconstr Surg. 2014;36:280.
17. Huang MH, et al. Evaluation of glycan/poly (vinyl alcohol) blend wound dressing using rat models. Int J Pharm. 2008;346:38-46.
18. Bryan J, et al. Moist wound healing: A concept that changed our practice. J Wound Care. 2004;13:227-228.