Overview of Dalethyne and other Topical Antiseptics for Wound Care

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A cascade of enzymes acting in union is involved in the natural wound healing pharmacology of humans making the process a lengthy one. This in turns necessitates new synthetic molecules effective in accelerating the wound healing process. The present review provides an overview of wound healing potential of the traditionally known compounds together with a comparison of the activity of the conventional compounds with respect to the dalethyne derivatives. Additionally, the present review summarises the antiseptic and the anti-microbial action of the conventional wound healing agents together with a comparison with the dalethyne derivatives. The review further indicates that the Dalethyne derivatives exhibit potent wound healing activity with respect to the traditionally known components which is attributed to their conducive anti-microbial action. However, the present review is an exhaustive one and also refers to some of the experimental data which has been observed in present laboratory experiments.
1. INTRODUCTION

Wide array of wound antiseptic has been used in wound care. With recent development of antimicrobial resistance, there is an urgent need in developing a new topical antiseptic. The purpose of this review is to study the characteristics of commonly used antiseptic in comparison with Dalethyne for wound care. The natural process of wound healing consists of 4 overlapping but well defined phases which are hemostasis, inflammation, proliferation and remodeling. Hemostasis is the first phase of wound healing and is a blood clot formed of thrombocyte aggregation and other blood cells (Enoch et al., 2006). Blood clot will provide a temporary extracellular matrix to facilitate cell migration. Inflammation phase involves migration of blood cells such as phagocytic neutrophils and macrophages to the wound location. These phagocytes will remove foreign debris while also releasing cytokines which will promote fibroblast migration and proliferation in later inflammation phase (Topman et al., 2013). Wound re-epithelization started in a few hours after wound formation and is a part of proliferation phase. This phase is marked with the formation of new blood vessels (angiogenesis and neovascularization), which will restore perfusion and maintain the formation of new tissue (Topman et al., 2013). This formation is supported by synthesis and deposition of extracellular matrix protein fragments such as collagen fiber by fibroblast and granulated tissue (Enoch et al., 2006). The final phase of wound healing involves collagen remodeling and the formation of scar tissue. Thus, a wound treatment agent need to protect wounded tissue from bacterial infection, reduce inflammation and induce cell proliferation to help in reconstruction of damaged tissue (Kulac et al., 2013). The optimal wound healing agent will protect the tissue from bacterial infection, reduce inflammation, and induce cell proliferation to help with the reconstruction of the damaged tissue (Kulac et al., 2013). It will ideally act as antioxidant because the free radical is considered as the main cause of inflammation in the wound healing process (Mohanty et al., 2012).

Proper healing of wounds, arising either from injury or from diabetes, using a suitable medication poses a severe problem over the ages. Various herbal products have been used since long time for wound healing. It has been reported that bandages and dressings soaked in natural honey keep the wound clean and stimulate the healing. Colloidal silver and Chinese herbal applications showed positive effects on faster healing (Siavash et al., 2015; Chen et al., 2010). Fatty acids have been shown to have intense effects on wound healing and infections (Alexander and Supp, 2014). Dalethyne (Dharshan, 2018) is a content of olive oil. The novel compound dalethyne is a combination of four key compounds of peroxide, anisidine, iodine and aldehyde obtained from a process of fatty acid segregation using high-defined oxygen; that brings functions as anti-microbial, fungicidal and virucidal. Investigations have revealed that dalethyne reduces inflammation in mice and accelerates wound healing (Erivna et al., 2017). The present review provides an overview of the various wound healing agents commonly used with special emphasis on the wound healing potential and the antiseptic action of the dalythene derivatives. However, the review is exhaustive and summarises the wound healing action of the dalythen derivatives based on the published data.

2. REVIEW

Some of the commonly used antiseptic agents have been reviewed in the present report emphasising their potential as wound healing agents. The review chiefly focusses on the effect of the Dalethynes derivatives in comparison to the convention antiseptics in terms of their wound healing effects. Extensive research has been done on te Dalythene derivatives to determine their potential as wound healing agents as well as their function as antiseptics. Table 1 provides a comparative analysis of the anti-microbial potential of the traditional antimicrobial agents together with the anti-microbial effect of the Dalythene derivatives. Additionally, Tables 2, 3 and 4 summarise the wound healing potential of the traditional compounds together with that of the Dalythene derivatives and provides a comparison of the exerted side effects and the contraindications.

Table 1: Antimicrobial activities of the wound healing agents

<table>
<thead>
<tr>
<th>Antiseptic agents</th>
<th>Staphylococcus aureus</th>
<th>Pseudomonas aeruginosa</th>
<th>Candida albicans</th>
<th>Clostridium perfringens</th>
<th>HSV-1</th>
<th>MRSA</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>NaCl</td>
<td>---</td>
<td>---</td>
<td>---</td>
<td>---</td>
<td>---</td>
<td>---</td>
<td>(Beam JW, 2006)</td>
</tr>
<tr>
<td>Chlorhexi-dine</td>
<td>√</td>
<td>√</td>
<td>√</td>
<td>√</td>
<td>---</td>
<td>---</td>
<td>(Payne et al., 1999); (Deck and Winston, 2012); (Cookson et al., 1991)</td>
</tr>
<tr>
<td>Povidone-iodyne</td>
<td>√</td>
<td>√</td>
<td>√</td>
<td>√</td>
<td>√</td>
<td>√</td>
<td>(Cooper R, 2004); (Deck and Winston, 2012)</td>
</tr>
<tr>
<td>Silver Sulfadiazine</td>
<td>√</td>
<td>√</td>
<td>√</td>
<td>√</td>
<td>√</td>
<td>√</td>
<td>(Cooper R, 2004); (Hermans MH, 2006); (Fong et al., 2005)</td>
</tr>
<tr>
<td>PHMB</td>
<td>√</td>
<td>√</td>
<td>√</td>
<td>√</td>
<td>√</td>
<td>√</td>
<td>(Kramer et al., 2018); (Sibbald et al., 2017); (Faby et al., 2013)</td>
</tr>
<tr>
<td>Dalethyne</td>
<td>√</td>
<td>√</td>
<td>√</td>
<td>√</td>
<td>√</td>
<td>√</td>
<td>(Darshan, 2018b, c)</td>
</tr>
</tbody>
</table>
### Table 2: Wound healing properties

<table>
<thead>
<tr>
<th>Antiseptic agents</th>
<th>Anti-inflammation</th>
<th>Pro-proliferation</th>
<th>Pro-remodelling</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>NaCl</td>
<td>---</td>
<td>---</td>
<td>---</td>
<td>(Beam JW, 2006)</td>
</tr>
<tr>
<td>Chlorhexidine</td>
<td>---</td>
<td>---</td>
<td>---</td>
<td>(Main RC, 2008)</td>
</tr>
<tr>
<td>Povidone-iodine</td>
<td>√</td>
<td>√</td>
<td>√</td>
<td>(Bigliardi et al, 2017); (Kramer et al, 2018)</td>
</tr>
<tr>
<td>Silver Sulfadiazine</td>
<td>√</td>
<td>√</td>
<td>√</td>
<td>(Geronemus et al, 1979); (Kramer et al, 2018); (Wong et al, 2009)</td>
</tr>
<tr>
<td>PHMB</td>
<td>√</td>
<td>√</td>
<td>√</td>
<td>(Goertz et al, 2011); (Gentile et al, 2012)</td>
</tr>
<tr>
<td>Dalethyne</td>
<td>NA</td>
<td>---</td>
<td>---</td>
<td>(Darshan, 2018a)</td>
</tr>
</tbody>
</table>

### Table 3: Application of the wound healing agents

<table>
<thead>
<tr>
<th>Antiseptic agents</th>
<th>Irrigation</th>
<th>Acute Wound</th>
<th>Chronic Wound</th>
<th>Burn Wound</th>
<th>Diabetic Ulcer</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>NaCl</td>
<td>√</td>
<td>---</td>
<td>---</td>
<td>---</td>
<td>---</td>
<td>(Beam JW, 2006)</td>
</tr>
<tr>
<td>Chlorhexidine</td>
<td>√</td>
<td>---</td>
<td>---</td>
<td>---</td>
<td>---</td>
<td>(Russel AD, 2003)</td>
</tr>
<tr>
<td>Povidone-iodine</td>
<td>√</td>
<td>√</td>
<td>---</td>
<td>---</td>
<td>---</td>
<td>(Kramer et al., 2018)</td>
</tr>
<tr>
<td>Silver Sulfadiazine</td>
<td>---</td>
<td>---</td>
<td>√</td>
<td>√</td>
<td>---</td>
<td>(Sibbald et al., 2017); (Kramer et al., 2018)</td>
</tr>
<tr>
<td>PHMB</td>
<td>√</td>
<td>√</td>
<td>√</td>
<td>√</td>
<td>√</td>
<td>(Eberlein and Assadian, 2010); (Sibbald et al., 2017); (Eberlein and Kanis, 2014)</td>
</tr>
<tr>
<td>Dalethyne</td>
<td>NA</td>
<td>√</td>
<td>√</td>
<td>√</td>
<td>√</td>
<td>(Darshan, 2018a)</td>
</tr>
</tbody>
</table>

### Table 4: Side Effects associated with the wound healing agents

<table>
<thead>
<tr>
<th>Antiseptic agents</th>
<th>Irritation</th>
<th>Allergy</th>
<th>Side Effect</th>
<th>Contraindication</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>NaCl</td>
<td>---</td>
<td>---</td>
<td>---</td>
<td>---</td>
<td>(Beam JW, 2006)</td>
</tr>
<tr>
<td>Chlorhexidine</td>
<td>√</td>
<td>√</td>
<td>Neurotoxic</td>
<td>Hypersensitivity,</td>
<td>(Deck and Winston, 2012)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Middle ear surgery</td>
<td></td>
</tr>
<tr>
<td>Povidone-iodine</td>
<td>---</td>
<td>√</td>
<td>Iatrogenic</td>
<td>Hypersensitivity,</td>
<td>(Kramer et al., 2018)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Hyperthyroid goiter, Herpetiform, dermatitis, Radioiodine treatment, Gastric lavage</td>
<td></td>
</tr>
<tr>
<td>Silver Sulfadiazine</td>
<td>√</td>
<td>√</td>
<td>Blood discaryasis</td>
<td>Hypersensitivity, Renal impairment, G6PD deficiency</td>
<td>(Caffee and Bingham, 1982)</td>
</tr>
<tr>
<td>PHMB</td>
<td>---</td>
<td>√</td>
<td>---</td>
<td>Hypersensitivity, Early pregnancy</td>
<td>(Kramer et al., 2018)</td>
</tr>
<tr>
<td>Dalethyne</td>
<td>---</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
<td>(Darshan, 2018b)</td>
</tr>
</tbody>
</table>

### 2.1 Normal Saline - NaCl 0.9%

Normal saline (from here will be mentioned as saline) consisting of sodium chloride (NaCl) diluted in sterile water with concentration of 0.9% (9g/L of water). Saline is commonly used for i.v. injection to treat dehydration or for external use such as wound irrigation. In wound irrigation, saline itself doesn't provide any significant benefit compared to sterile water. Saline being an easy to use antiseptic is preferred for wound irrigation (Beam JW, 2006).

### 2.2 Chlorhexidine

Chlorhexidine is a biguanide antiseptic with 2 common formulations: (a) chlorhexidine gluconate (CHG) in alcohol based formulation and (b) chlorhexidine digluconate (CHD) in water based formulation.
Chlorhexidine is worked in a physiological pH (pH: 5.5-7.0) by releasing a chlorhexidine cation from chlorhexidine salt. This cation is readily adsorbed by negatively charged bacterial cell walls, causing membrane disruption. Due to its pH dependent mechanism of action, chlorhexidine can be deactivated by other skin cleansers (Deck and Winston, 2012).

The antimicrobial activity of chlorhexidine is effective against a broad spectrum of pathogens but especially effective against gram positive cocci such as *Staphylococcus aureus*. Chlorhexidine is also effective against gram negative rod and cocci such as *Pseudomonas aeruginosa* but not to the extent of its effect against positive gram bacteria (Payne et al, 1999). Routine usage of chlorhexidine has also proven to be effective against sporal bacteria due to its persistent effect, resulting in a similar effect such as alcohol disinfection but requiring longer time (McDonnell and Russell, 1999). Chlorhexidine is not effective against viral infection (Deck and Winston, 2012) and not recommended against MRSA due to developed resistance (Cookson et al, 1991).

Since its invention in 1946, chlorhexidine has been used in the medical world as an antiseptic. Chlorhexidine has been used for hand wash and preoperative disinfection but use of chlorhexidine in wound treatment is limited for wound irrigation (Russel, 2003). Chlorhexidine failed to provide any other benefit in wound healing process other than its antiseptic properties and might even prove detrimental if used in cases other than for irrigation (Main, 2008). Chlorhexidine can't be used for middle ear surgery and neurosurgery due to its neurotoxicity (Deck and Winston, 2012).

### 2.3 Povidone-iodine

Povidone-iodine (PVP-1) is an idophore antiseptic commonly used for topical disinfection. As its name suggest, PVP-1 is a chemical complex of povidone, hydrogen iodide and iode. The bacteriocidal action of PVP-1 is attributed to the presence of free iodine provided in PVP-1, while povidone bonded to iodine provides a slow release of free iodine to reduce toxicity and side effect. Free iodine will alter membrane structure and prevent hydrogen bonding of pathogens. It has a broad spectrum of antiseptic activity and is frequently used for treating minor wound and surgical disinfection (Cooper, 2004). PVP-1 is effective against a broad spectrum of bacteria including gram positive, negative and even MRSA. Aside from bacteria, PVP-1 is also effective against other kind of pathogen including mycobacteria, yeast, dermatophyte, encapsulated and unencapsulated virus and protozoa. PVP-1 is also effective against bacterial spore in a prolonged application (Deck and Winston, 2012).

PVP-1 doesn't provide any benefit in wound healing process compared to other antiseptics such as PHMB (polyhexamethylene biguanide) and silver. Even so, PVP-1 doesn't cause as much pain during dressing change compared to silver dressing. In general, wound healing process using PVP-1 takes around 2-3 weeks (Kramer et al, 2018). Further, PVP-1 shows anti-inflammatory activities which help the wound healing process (Bigliardi et al, 2017). Usage of PVP-1 for longer than 7 days is not recommended because prolonged use of PVP-1 may alter thyroid function. If there is no other option for antiseptic dressing, routine thyroid function test should be conducted in a prolonged use. Extra attention should be given in application for pregnant woman, infant ageing less than 6 months and patient with thyroid disease. Contraindications for PVP-1 include hypersensitivity, hyperthyroid goiter, dermatitis herpetiformis, undergo radiiodine therapy or peritoneal lavage (Kramer et al, 2018).

### 2.4 Silver Sulfadiazine

Silver sulfadiazine (SSD) is a topical antibiotic commonly used for wound dressing, especially to prevent infection in burns. Antibiotic property of SSD is attributed to the presence of silver ions and sulfadiazine released when in contact with aqueous environment such as bodily fluid in burn wound. Silver ions are readily absorbed by bacteria and bind to negatively charged proteins and nucleic acids resulting in disruption of cell membrane and internal function. Sulfadiazine also helps by inhibiting dihydropteroate synthase enzyme (Cooper, 2004).

The antibacterial activity of silver is effective against both gram positive and negative bacteria (Hermans, 2006). Due to the universal antibacterial mechanism of silver by causing proton leakage, silver also shows broad spectrum of antimicrobial activity against yeast and virus. Silver is especially effective in preventing the colonization of *P. aeruginosa* that frequently infect burn wound (Fong et al, 2005). Complimenting antimicrobial property of silver, SSD also showed positive properties to help in wound healing process. In pig with clean wound, application of SSD dressing increased the epithelialization rate by 28% (Geronemus et al, 1979). Usage in human showed increase in quality of care by reducing the number of bacterial count, increased healing and decrease in pain. Silver is also capable of inhibiting wound odor and secretion (Kramer et al, 2018).

Silver nanoparticles are also known to have anti-inflammatory properties which help in wound healing process (Wong et al, 2009). Due to its activation mechanism, silver is best used for healable wound with high risk of colonization such as burn wound. Silver is not recommended to be used for maintenance wound because the main goal of the treatment is to reduce moisture which will prevent the activation of silver's antimicrobial activity (Sibbald et al, 2017). However, silver is not recommended to be used for longer than 14 days or as a prophylaxis (Kramer et al, 2018). Side effect that may occur during usage of SSD can be caused by reaction towards sulfonamide. These reactions include blood diascardiasis, hypersensitivity, steven-johnson syndrome, toxic epidermal necrolysis and exfoliative dermatitis. Reaction can also occur in gastrointestinal tract, liver, central nervous system and kidney. Usage of SSD in patient with G6PD deficiency can cause hemolytic reaction (Caffee and Bingham, 1982).
2.5 Polyhexamethylene-Biguanide

Polyhexamethylene-biguanide (PHMB) is a biguanide antibiotic used for disinfectant and antiseptic. PHMB is a polymer with positive charge which helps to deliver the active component to the negatively charged bacterial wall. This will cause the loss of fluidity in bacterial cell wall, causing the dissolution of bacteria. It is essentially a better version of chlorhexidine, providing the same efficacy but with better safety and tolerability (Kramer et al., 2018). PHMB is effective against a broad spectrum of pathogens including positive and negative gram bacteria, yeast and virus (Sibbald et al., 2017). Further, PHMB is able to prevent and treat infection from bacteria that commonly infect wounds such as P. aeruginosa, S. aureus and even MRSA (Fabry et al., 2013).

In addition to its antimicrobial activity, PHMB also helps in the process of wound healing (Sibbald et al., 2017). During both in vitro (Hubner et al., 2010) and in vivo studies (Perez et al., 2010) PHMB is able to destroy biofilm and speed up wound healing process as reflected in an increased capillary density and increase in arteriole diameter (Goertz et al., 2011). PHMB also showed anti-inflammatory activities in wound healing process (Gentile et al., 2012). PHMB has a wide array of formulation and application. PHMB is commonly available in the form of solution, hydrogel and for wound dressing (Eberlein and Assadian, 2010). PHMB is best used for chronic exudative wound with a high risk of bacterial colonization (Sibbald et al., 2017). PHMB foam dressing formulation is especially effective when used in conjunction with negative pressure wound treatment in treating diabetic ulcer and burn wound (Eberlein T and Kanis J, 2014). Side effect rarely occurs in PHMB usage but may include hypersensitivity. Aside from hypersensitivity, contraindication results if given to pregnant woman with less than 4 months old pregnancy (Kramer et al., 2018).

2.6 Dalethyne

Olive oil is composed of 98% triglycerides, including predominantly mono unsaturated oleic acids, their anti-inflammatory properties being proven to be essential for skin maintenance. Dharshan developed Dalethyne based on rearrangement of the structure of olive oil based on substituent variation and reported 18 different dalethyne derivatives by varying the side chains of the parent scaffold (Darshan, 2018a). These 18 compounds have been categorised into four different groups, namely peroxide, aldehyde, iodine and anisidine.

Iodine, peroxide, and anisidine are compounds that play a role in the epidermis and dermis level and work in cleaning the wound area (killing bacteria), so that a conducive environment is created for the repair process. Peroxide has the ability to trigger the performance of macrophages and neutrophils, which play a role in engulfing bacterial cells, dying cells, and dead cells. In the process, the macrophages will secrete pro-inflammatory cytokines such as IL-6, TNF-α, and IL-18 which in turn maximize the inflammatory response in the body. The three cytokines play essential role in the inflammatory process and the wound area is cleared of dead bacterial cells and body cells in a faster time than without assistance of the cytokines. IL-6 will trigger an acute phase response, where this process will trigger the formation of fibrin to cover the wound area, so that bacteria cannot enter the wound (Desborough 2000). Of the four types of compounds contained in Dalethyne, only the aldehyde compounds are able to infiltrate and work in the hypodermic layer. When a wound occurs, the released ATP or extracellular ATP in the injured tissue has reduced ability to trigger the wound healing process. So, the presence of the aldehyde in the hypodermic area will trigger extracellular ATP, so that more ATP will be released from the surrounding cells through the process of sugar metabolism. High ATP can induce the body's response to injuries by activating the release of the growth factors such as TGF-α, EGF, βFGF etc. The higher the ATP in the environment, the higher is the growth factor level. EGF and βFGF will promote reepithelialization and induce collagen and keratin synthesis (Laato et al., 1987). TGF-β, TNFα, and IL-1 will enter hypodermis and trigger collagen synthesis. Collagen in the hypodermis will rise to the upper layer. Subsequently, the growth factors trigger the occurrence of angiogenesis and granulation. The increase in collagen concentration in the dermis and epidermis layer is conducive to the initiation of repair processes such as epithelialization, fibroplasia and neovascularization (Velnar et al., 2009).

In chronic wounds, necrotic tissue around the wound causes inhibition in the process of repairing the wound (because the body is unable to do autolysis), so the tissue needs to be debrided. Accumulates dead cells, pathogens, and exudates take place in the necrotic tissues. Debridement resulting from effective application of topical drugs to chronic wounds has a positive impact facilitating induction of a process of wound repair. However, the negative impact of debridement is to open the entry pathway of bacteria into the blood vessels, which affects other complications. MRSA is also found in areas of chronic injury, especially in necrotic tissue in diabetic foot disease, while entry of the bacteria into the blood vessels leads to sepsis (Bowling et al.; 2009). The use of Dalethyne may minimize areas treated with debridement and having a broad-spectrum antibacterial abilities (can kill groups of bacteria that are resistant to antibiotics such as ESBL, KPC, and MRSA) without causing resistance, dalythene can work effectively in healing skin due to chronic wounds. Herewith, we summarized some studies both experimental (in vivo and in vitro) as well as clinical study in involving the use of Dalethyne as antiseptic and wound healing agent.

2.6.1 Antiseptic action of dalythene

Several studies have been conducted to explore the antiseptic activities of Dalethyne ranging from in silico, in vitro and in vivo studies.
In silico analysis:

Dalethyne cream facilitates the wound healing process by activating the molecular mechanism involved in the wound healing process. Dalethyne has been predicted to be able to lower inflammatory agents such as MMP-9 and COX-2. It is also able to reduce oxidative stress, modulate the expression of growth factors (FGF-2 and TGF-β1) and inflammation mediators (IL-1β and IL-6) (Darshan, 2018a).

According to the docking result of the 18 Dalethyne derivatives, methyl 8-octadecanoate has a conducive inhibitory activity against C. albicans and P. aeruginosa. Methyl palmitate has a good activity against HPV-1 (Herpes simplex viruses) and methyl-6, 6-dimethoxyoctanoate shows excellent against HPV-1 (Human papillomavirus). Dalethyne exerts potential activity against Candida albicans and Candida glabrata by inhibiting the fungi’s enzymatic activity resulting in malnutrition of the pathogen. Dalethyne also exhibits good inhibitory potential against bacteria especially Pseudomonas aeruginosa and MRSA. Dalethyne showed little activity against HSV-1, HSV-2 and HPV-16 but showed most promising action against HSV-1 (Darshan observation, Report UI. Study in Silica of Dalethyne against Wound Healing Bacteria).

Based on the variance of bacteria tested, Pseudomonas aeruginosa, Escherichia coli and Klebsiella Pneumonia constituted the gram-negative bacteria group, while MRSA, Staphylococcus aureus, Streptococcus pyogenes and Aerococcus viridans constituted the gram-positive bacteria group. It has been reported that Methyl linoleate can inhibit four bacteria namely, Staphylococcus aureus (with penicillin binding protein mechanism and sortase mechanism), Streptococcus pyogenes, Aerococcus viridans, and Escherichia coli. Again, Methyl myristate shows activity by inhibiting bacteria like Staphylococcus aureus with DNA gyrase B mechanism, Streptococcus pyogenes, Aerococcus viridans, and Escherichia coli. On the other hand, Dimethyl azelate can inhibit MRSA, Staphylococcus aureus with penicillin binding protein mechanism and Klebsiella 16neumonia. Methyl 11-eicosanate is also capable of inhibiting bacteria like Pseudomonas aeruginosa, Staphylococcus aureus with penicillin binding protein mechanism and Klebsiella 16neumonia. From 18 Dalethyne compounds, 13 compounds have been found to inhibit 7 bacteria (gram-negative and gram-positive), thereby exhibiting excellent potential as broad-spectrum antibacterial agent (Darshan observation, In silica study of wound healing mechanism, antibacterial, antifungal and antiviral activities of Dalethyne).

In vitro studies analysis:

Dalethyne is effective against a wide array of pathogens commonly found in wound infection. Dalethyne is able to inhibit the formation and destroy biofilm produced pathogens, requiring lower concentration to inhibit bacterial growth compared to inhibition or destruction of biofilm (Darshan observation, Effectivity of Dalethyne against biofilm).

As an antiseptic, Dalethyne is effective against Pseudomonas aeruginosa, MRSA, Clostridium perfringens, Candida albicans, Staphylococcus aureus and Streptococcus pyogenes. Dalethyne at the 30% concentration has a phenol coefficient value to Salmonella typhi bacteria of 3.63, while for Staphylococcus aureus bacteria of 4.44. These results prove that Dalethyne at 30% concentration has antiseptic effects against Salmonella typhi bacteria 3.63 times better than phenol, while for Staphylococcus aureus bacteria its ability is 4.44 times better than that of phenol. The results for the percentage of bacteria killed indicate that this compound is most effective to eliminate Pseudomonas aeruginosa and Clostridium perfringens. Its effectiveness for Candida albicans is not as good as to bacteria mentioned before since it takes long contact time to be able to give effect as expected (Darshan KS, 2018b, c). Dalethyne is also effective against other multiple drug resistant organisms such as ESBL E. coli, ESBL K. pneumonia and Carbapenem resistant K. pneumonia (Darshan observation, Daleathyne: effectiveness study on microbes which cause nosocomial infection an in vitro study).

In vivo study analysis:

Dalethyne has been tested on incised wound on rat infected with clinical isolate of bacteria including: S. aureus, S. epidermidis, S. pyogenes, P. aeruginosa, A. baumanii, MRSA, ESBL E. coli, ESBL K. pneumonia, Carbapenem resistant K. pneumonia and candida fungus. Topical application of Dalethyne on infected wound incision resulted in 0 mortality by day-7, together with increased macroscopic and microscopic wound healing. Increased microscopic wound healing is indicated by perfect epithelialization, sufficient fibroplasia, increased vascularization and no scar by day-7. Infection had lengthened the inflammation period, distracted the fibroplasia and neovascularization process, resulting in longer duration of wound healing process (Darshan observation, Dalethyne effectivity study on infected incised wound of rattus norvegicus).

2.6.2 Wound healing

In studies conducted on rat, topical application of Dalethyne product on incised skin provided faster wound healing compared to placebo. Placebo consisted of vehicle cream without Dalethyne. In placebo group, erythema and edema still occurred on the 3rd day, while the incised wound has dried up on the 6th day and was covered in crustae. In Dalethyne group, erythema and oedema was abated on the 3rd day, while majority of the incised wound closed up on the 6th day. Dalethyne increased the rate of erythema and edema abatement and wound closing compared to placebo. In a study conducted on rat, topical application of Dalethyne on incised wound on rat tend to increase macroscopic and microscopic wound healing by day-7. Microscopic wound healing indicated by perfect epithelialization, sufficient fibroplasia, increased vascularization and no scar was left by day-
2.6.3 Toxicity and Clinical studies

Several in vivo studies have been conducted to explore the possible toxicity and side effect caused by topical application of Dalethyne. On study of intramuscular LDSO acute toxicity using 4ml/kg BW dose, intramuscular injection of Dalethyne in rat's thigh did not cause any side effect or mortality (Darshan observation, LDSO Acute toxicity study of intramuscular injection of Dalethyne). Topical application of Dalethyne on incised wound inn rat didn't cause any mortality until day-7. Further, topical application of Dalethyne product on rabbit's intact skin doesn't cause irritation or hypersensitivity reaction and also no internal organ toxicity on both intact and incised skin. The acute skin irritation study of Dalethyne in all 3 doses of concentration (20%, 30% and 40%) in rabbit showed no sign of skin irritation, similar to control/vehicle (glycerine) (Darshan observation, Acute skin irritation study of Dalethyne in rabbit). Further, clinical study has been conducted for the usage of Dalethyne in human. Dalethyne could be used for grade 0-1 diabetic foot ulcer, dry skin, acne and mild burn.

3. CONCLUSION

The present review provides a precise summary of the various wound healing agents that are traditionally used for the treatment of wounds. In addition, a comparison table has been presented in the present review to determine the wound healing potential of the Dalethyne derivatives over the traditionally known components. The antiseptic action of the compounds have also been analysed in the present review which adds to the wound healing potential of the different components. Most of the traditionally known components exhibit limitation in inhibiting all the bacteria that are commonly known for infecting the wounds. However, the Dalethyne derivatives have been found to exert potent against all the commonly identified bacteria that have been indicated in infecting wounds. Further, observations from different types of studies as well as clinical trial analysis indicates that the Dalethyne derivatives have proved to exhibit potent anti-microbial as well as antiseptic action which in turn accounts for the improved wound healing potential of the Dalethyne derivatives.

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Conflict of Interest

The author has none to declare.

REFERENCES


