Research Article

Formulation of Microemulsion containing *Nigella Sativa* Honey and Propolis and Evaluation of its Burn Healing Potential

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ABSTRACT

The objective of present study was to develop and characterize the microemulsion system for topical delivery of *Nigella sativa* honey and Ethanolic extract of propolis (EEP), investigate its antibacterial activity and determine its burns healing potential. Microemulsions after being prepared by mixing appropriate amount of surfactant (Tween 20), co surfactant (ethanol), oleic acid as an oil phase and water as an aqueous phase, were evaluated regarding pH, viscosity, conductivity, particle size and stability. All Formulations having mean pH comparable to skin pH caused no irritation to skin. Conductivity of these formulations found from 19.67±0.57 to 112±1 µS /cm with mean viscosities at 20, 50 and 100 rpm ranging from 39.1667±0.153 to 62.50±1.323cps, 104.67±1.49 to 118.6±0.36cps and 169.36±0.47 to 183.60±1.9cps respectively. Particle size of microemulsions varying from 125.26±4.37nm to 190.91±2.26nm found comparable to microemulsions droplet size, 20 to 200nm. These results showed that physicochemical properties of microemulsion depend upon percentages of mixture of surfactant, co surfactant, oil and water. Results of drug contents and stability study showed that DM_8 microemulsion having greatest amount of honey and EEP, remain stable even after 45 days. Mean zone of inhibition of DM_8 formulation was 26±1 mm against *Staphylococcus aureus* which was determined by well diffusion method. In vivo study results established that microemulsion containing *Nigella sativa* honey and EEP have faster rate of healing burns than Silver Sulphadiazine (SSD) cream and blank microemulsion. Final percentage wound contraction caused by drug loaded microemulsion and SSD cream found to be 99.305± 0.51% and 89.075± 2.28% respectively.

Keywords: Burns, Ethanolic extract of propolis, Microemulsion, Nigella sativa honey, Rats, Silver Sulphadiazine (SSD), *Staphylococcus aureus*, Zone of Inhibition (ZI).

INTRODUCTION

Burns are tissue lesions which are caused by exposure to flames, liquids, chemicals, hot surfaces and radiations. They directly damage the mechanical barrier, neutrophil function and immune response due to which burnt patients are at high risk of developing wound infections, ventilator associated pneumonia and sepsis. As burns provide a good environment for the growth of microorganisms, they are colonized with mixed bacterial flora within hours, leading to delay in healing process of wounds and causing infection. Pathogenic microorganisms, *Staphylococcus aureus* and *Pseudomonas aeruginosa,* are predominant in burn wounds. To minimize the colonization of these microorganisms and infection caused by them, it is important to develop conditions that are unfavorable for the microorganisms and favorable for the host repair mechanisms. Topical antimicrobial agents like antibiotics and antiseptics provide these facilities with certain limitations. Systemic antibiotics can be used for the treatment of burns, but these have low penetration rate into death tissue and microorganisms develop resistance against them. Antiseptics also have bactericidal action but their burn healing process is very slow.[1-3]

However, honey and propolis have been found very good alternative of antibiotics and antiseptic, as they improve the healing rate of mild to moderate superficial and partial thickness burn infections. They are herbal remedies and unique gift of nature. Honey has water and sugar as its major constituents with variable amount of hydrogen peroxide, free radical, volatile organic acid, phenolic compounds, alkaloids, anthraquinones, glycosides, saponins, flavonoids, tannins, reducing compounds and bee waxes. Propolis is a resinous substance which is obtained from different parts of plants like exudates of buds, leafs and barks by *Apis mellifera* honey bees and is also present in extracted honey. It contains wax, resin, vegetable balsam, essential and aromatic oil, flavonoids and organic debris. Having this enriched composition, honey and propolis are very effective in the treatment of skin infection and have antimicrobial, anti-inflammatory, analgesic, and burn healing properties, thus promoting the re-epithelization process in wounds. Their flavonoids contents boost the immunity and decrease the risk of allergic reaction in burned patient.[3-7]

There are various types of formulation available for the topical administration of drugs like cream, ointment, gel, microemulsion. However microemulsion system is preferred for topical delivery of drugs as it is transparent, thermodynamically stable and can increase the topical delivery of both water soluble and lipid soluble drugs due to its high solubilization capacity, low viscosity, small droplet size, high drug loading capacity, penetration enhancing effect of the individual components and entry

of the components in the skin as monomer, thereby increasing the solubility of the drug in the skin and transport of drug in controlled manner. Microemulsion system consists of an oil phase, aqueous phase, surfactant and co surfactant. Surfactants and co surfactants stabilize a microemulsion by making an interfacial film and make it in single phase. These also enhance skin permeation of drug by increasing the solubility of drug in skin.[8]

The aim of present study was to formulate the microemulsion containing *Nigella sativa* Honey and Ethanolic extract of propolis and determine its antimicrobial activity against *Staphylococcus aureus*. In vivo study of microemulsion was also conducted and its burn healing potential was determined on Albino rats. Results of antimicrobial activity and burn healing potential of microemulsions were compared with marketed Silver sulphadiazine cream.

MATERIALS AND METHODS

Material

Nigella sativa honey and propolis were gifted by National agriculture and research centre (NARC) Islamabad. Tween 20, Tween 80, Isopropylmyristate were bought from Panaeric Hanco Lahore. Propylene glycol and Oleic acid were gifted by the Avonchem Limited. Sesame oil, Sunflower oil and soya bean oil (Market) were bought from local market. Ethanol was bought from BDH Laboratories Lahore. Quercetin was gifted by the WTO Department, University of veterinary and animal sciences Lahore. Staph 110 agar media was taken from Microbiology Department University of Veterinary and Animal Sciences. Marketed 1% Silver sulphadiazine cream was purchased from Pharmacy

Microorganisms

Staphylococcus aureus colony from Microbiology Department, University of Veterinary and Animal Sciences, Lahore, Pakistan.

Animals

Albino rats were obtained from University of Veterinary and Animal Sciences, Lahore, Pakistan.

Methods

Preparation of Ethanolic extract of propolis (EEP)

500 gram of propolis was macerated in 1 to 1.5 liter of 95% ethanol for 10 days. This mixture was shaken twice a day. After 10 days macerated material of propolis was filtered by coffee filter paper to get filtrate. The filtrate was evaporated under reduced pressure at 40^0C in rotary evaporator to get the concentrated extract of propolis (EEP). The concentrated extract was collected in tightly closed container and stored in freezer in order to prevent bacterial growth.[9]

Solubility studies

The solubility of EEP was determined in different oils, surfactants and co surfactants to select the suitable oil and surfactant which could provide excellent skin permeation rate of drug. An excess amount of drug was added to 5ml of each solvent and was shaked for 72 hours at 20^0C. The suspension was filtered through membrane filter paper (0.45µm) and concentration of drug was determined in the filtrate with the help of HPLC.[10, 11]

Construction of Pseudo ternary phase diagrams

Pseudo Ternary phase diagrams were constructed to obtain the concentration ranges of components for the formation of microemulsion. The system was consisted of an oil phase, surfactant, co surfactant and aqueous phase. 1:1, 2:1 and 3:1 ratios of surfactant and co surfactant (Smix) were used for the development of pseudo ternary phase diagram. The ternary phase diagrams were constructed using water titration method at ambient temperature. For each phase diagram, 1:9, 2:8, 3:7, 4:6, 5:5, 6:4, 7:3. 8:2, 9:1 ratios of screened oil and Smix were used. These mixtures were tittered drop by drop with filter de ionized water under magnetic stirring. The concentration or amount of water at which transparency-to-turbidity transitions occurred was considered as the end point of titration. Area of microemulsion was determined by back titrating it. Immediate clear point before turbidity was considered as microemulsion. Major variables which affect the properties of microemulsions were percentages of mixture of surfactant and co surfactant (% Smix), percentages of oil (% oil) and water percentage (% water). Nine different microemulsions were prepared with different percentages of Smix (56, 46, and 36), Oil (25, 15, and 5) and water (14, 24, 34, 44, and 54).[12-14]

Preparation of Microemulsions

The surfactant and co surfactant were blended for 5 minutes to get the surfactant mixture (Smix 2:1). Screened oil was added in the Smix mixture and blended for 5 minutes. 5% concentrated EEP and honey (1:1) was added into mixture of oil and Smix and mixed under magnetic stirrer at room temperature until it was dissolved. Finally, an appropriate amount of water was added in the above mixture drop by drop under magnetic stirring. This mixture was stirred for 30 minutes to get microemulsion.[12]

Characterization of Microemulsion

Physical appearance

Appearance and clarity of microemulsion was determined by visual examination in terms of phase separation and transparency.[15]

Centrifugation

Resistance of microemulsion to phase separation was determined by conducting centrifugation test. The

centrifugal test was performed at 10000 rpm for 30 minutes by placing the 5 gram of sample in centrifugal tubes.[16]

pH

The pH of microemulsion was determined by a pH meter (Hanna H 19812) at 25°C.[17]

Conductivity

Electrical conductivity of microemulsion was measured using conductometer (M.Milwaukee) at ambient temperature.[15,18]

Viscosity

The viscosity of optimized microemulsion was determined using Brookfield viscometer at 25°C.[15]

Droplet size

The average droplet size of microemulsions was measured using a Zeta sizer.[15, 19]

Drug contents

Drug contents (flavonoid [quercetin] of propolis and *nigella sativa* honey) in microemulsions were determined by some modification of HPLC method given by Sultana and Anwar. An HPLC (model LC-20A, Shimadzu, Kyoto Japan) was used for this experiment. Buffer system contained 3% trifluoroacetic acid (TFA). Mobile phase was consisted of 50% buffer, 20% methanol and 30% acetonitrile. Detection was performed at 360nm by running the mobile phase at the rate of 1.0ml/min at 30°C.[11]

Stability study

The physical stability of microemulsion was evaluated by visual inspection such as by phase separation, transparency, drug precipitation and color change. Three batches of microemulsion were stored at 4°C, 25°C and 45°C for 45 days and examined for physical stability. [15, 20]

Antimicrobial activity

Zone of inhibitions of EEP, honey, blank microemulsion, microemulsion containing 5% concentrated EEP and honey and marketed silver sulphadiazine cream were determined against Staphylococcus aureus by well diffusion method. Petridishes containing 25ml of Staph 110 agar media was used. Five well (5 mm diameter) were cut into the agar by cork borer. Then agar media was seeded with 24 hour old culture of *staphylococcus aureus* by sterile cotton swab. 1 ml of each sample was applied in each well. Incubation was performed at 37°C for 24 hour. Antibacterial activity of samples was based on diameter of zone of inhibition.[2, 9]

In vivo study

Animals

Albino rats were used for *in vivo* study of microemulsion containing *Nigella sativa* honey and concentrated EEP. Sixteen rats were used for this study. Rats were divided into 4 groups. Their backs were properly shaved to expose their skin. Each group was placed in individual cages and controlled lightening condition and temperature (24 ±2°C) was maintained. Animals were also properly supplied with water and food.[21]

Thermal burn experimental models

Initially 16 animals were weighted and anesthetized with thiopental (40mg/kg body weight). Thermal injury was made with solid steel bar which was 12 mm in diameter, previously heated in boiling water for 20 seconds. The temperature of boiling water was maintained at 100°C. The bar was maintained in contact with back skin of animal for 20 seconds. The pressure exerted on the animal skin corresponded to the mass of 51 g of steel bar which was used in the burn induction.[21]

Treatment of burned rats

After 24 hours of thermal injury, Group 1 was treated with microemulsion of *Nigella sativa* honey and EEP; Group 2 was treated with blank microemulsion (without effective agent); Group 3 served as positive control and it was treated with 1% silver sulphadiazine cream and Group 4 served as negative control and no topical agent was applied on it. Formulations were applied twice daily on first three groups.[22]

Quantification of wound healing

In order to quantify the rate of wound healing, the size of lesions was determined on 3rd, 7th, 10 th, 14 th and 20 th day by tracing a wound margin on transparent plastic sheet. The lesion body area was displayed in mm^2. Wound contraction was expressed as reduction in percentage of original wound size. Wound contraction was determined by the formula:

%wound contraction on day X = [(area on day 1 – open area on day X)/area on day 1] × 100. [2, 21, 22]

Statistical Method

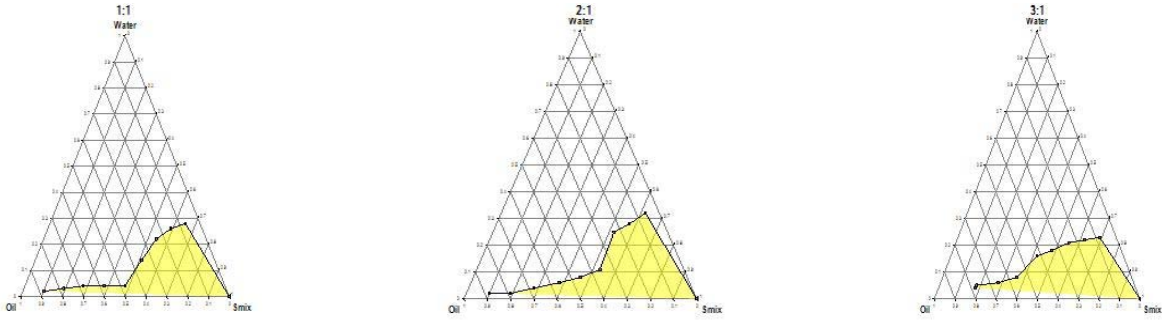
All the experiments were repeated three times and data were expressed as mean value ±SD. Statistical data were analyzed by one way analysis of variance (ANOVA) and $p<0.05$ was considered to be significant with 95% confidence interval.

RESULTS AND DISCUSSION

In this study oleic acid was selected as an oil phase because EEP (lipophilic) was only soluble in oleic acid and insoluble in other oils. Solubility of concentrated EEP was higher in Tween 20 and ethanol. Tween 20 also showed very good miscibility with oleic acid. Due to high solubility of drug in tween 20 and ethanol, these were selected as a surfactant and co surfactant for the preparation of microemulsion (Table 1). Honey was only soluble in water so water was selected as an aqueous phase.

Table 1: Solubility of EEP in different oils, surfactants and co surfactants (Mean ± SD)

	Excipients	Physical appearance	Solubility (mg/ml) Mean± SD
Oil	Isopropyl myristate	Immiscible, Small globules	–
	Oleic acid	Completely soluble	2.36±0.18
	Olive oil	Immiscible, Large globules	–
	Sunflower oil	Immiscible	–
	Sesame oil	Immiscible	–
	Soya bean oil	Immiscible	–
Surfactants	Tween 20	Soluble	18.7±0.45
	Tween 80	Soluble	9.3± 0.5
Co- Surfactants	Ethanol	Soluble	30± 0.65
	Propylene glycol	Soluble	6.46±0.11

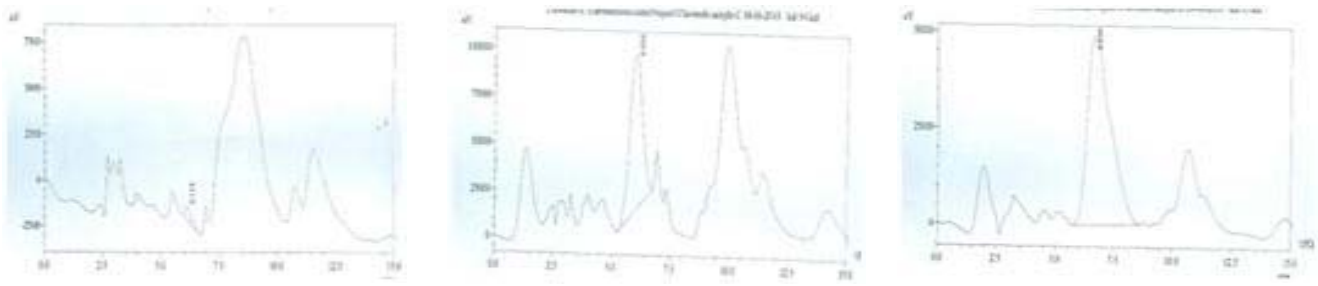


A **B** **C**

Figure 1: Pseudo-ternary phase diagram showing microemulsion region of Smix (Tween20: ethanol), oleic acid/ water at 25°C with different ratio of Smix (Surfactant: Co surfactant) **A**. 1:1 **B**. 2:1 **C.** 3:1 ratio of surfactant and co surfactant.

Table 2A: Composition of blank microemulsions (Smix 2:1), their physical appearance and phase behavior after 24 hours

Formulation code	Oil (%)	Smix (%)	Water (%)	Appearance	Phase behavior
BM_1	25	56	14	Transparent	Phase separation
BM_2	25	46	24	Turbid	Phase separation
BM_3	25	36	34	Turbid, Gel formed	Phase separation
BM_4	15	56	24	Transparent	No phase separation
BM_5	15	46	34	Transparent	Phase separation
BM_6	15	36	44	Turbid	Phase separation
BM_7	5	56	34	Transparent	No phase separation
BM_8	5	46	44	Transparent	No phase separation
BM_9	5	36	54	Transparent	No phase separation



A **B** **C**

Figure 2: HPLC Peaks of flavonoids contents of microemulsions containing 5% honey and propolis **A**. HPLC chromatogram of DM4, **B**. HPLC chromatogram of DM_7, **C**. HPLC chromatogram of DM_8

Table 2B: Composition of Drug loaded microemulsions (Smix 2:1), their physical appearance and phase behavior after centrifugation

Formulation code	Oil (%)	Smix (%)	Water (%)	Honey (%)	EEP (%)	Appearance	Phase behavior
DM_4	15	56	24	2.5	2.5	Transparent	No phase separation
DM_7	5	56	34	2.5	2.5	Transparent	No phase separation
DM_8	5	46	44	2.5	2.5	Transparent	No phase separation

Table 3: Average pH, Conductivity, viscosity and droplet size of blank and drug loaded microemulsion

Tests		Formulation Code	Blank microemulsion BM	Drug loaded microemulsion DM
pH Mean± SD		F_4	5.51±0.1	5.2±0.1*
		F_7	5.13±0.05	4.93±0.05*
		F_8	5.1±0.05	4.86±0.05*
Conductivity σ (µS /cm) Mean± SD		F_4	0.06±0.05	19.67±0.5*
		F_7	31±1	60.67±1.15*
		F_8	80.33±0.57	112±1*
Viscosity Mean± SD	20rpm	F_4	46.33±1.15	39.16±0.15*
		F_7	64.33±1.15	61.9±1*
		F_8	65.20±0.3	62.50±1.32*
	50rpm	F_4	111.67±1.5	104.67±1.49*
		F_7	120.67±1.5	115.63±0.55*
		F_8	121.67±0.5	118.6±0.36*
	100rpm	F_4	174.5±1.5	169.36±0.47*
		F_7	185.6±1.18	177.73±2.3*
		F_8	189.76±0.68	183.60±1.9*
Droplet Size nm Mean± SD		F_4	121.46±4.65	125.26±4.37 ns
		F_7	139.8± 4.35	146.25±4.20 ns
		F_8	186.5±2.31	190.91±2.26 ns

*Significant, ns: Non significant

The pseudo ternary phase diagrams of microemulsion system, which was composed of oleic acid as an oil , tween 20 as a surfactant, ethanol as a co surfactant and water as an aqueous phase has been shown in Figure 1 with different ratios of surfactants and co surfactants (1:1, 2:1, 3:1). The shaded area of phase diagram indicated microemulsion region while outside region indicated turbid region. In this study Pseudo ternary phase diagram having 2:1 ratio of tween 20 and ethanol (Smix) was selected for the preparation of microemulsion because it has largest microemulsion region as shown in Figure 1. This selection was consistent with previous study in which large microemulsion region was developed using 2:1 ratio of tween 20 and ethanol. This study was also present in close agreement to past study in which 2:1 ratio of tween 20 and ethanol was used for the preparation of natural microemulsion of walnut and turmeric. Previous studies also showed that microemulsion which was prepared using 2:1 ratio of tween 20 and ethanol had greater permeation rate across the skin in ex vivo study.[15, 23] The compositions of drug loaded microemulsions, their physical appearance and phase behavior are given in Table 2A.

BM_4, BM_7, BM_8 and BM_9 microemulsions were selected for further study because these were transparent having no phase separation after the period of 24 hours. These formulations were subjected to centrifugal test. BM_9 was rejected after this test because phase separation was occurred in it. Drug was loaded in selected blank microemulsions and centrifugal test was performed on them to check their stability (Table 2B).

Blank microemulsions (BM) had pH values from 5.1±0.057 to 5.51±0.1. pH of all these formulations were fall in the range of pH of skin (4.5 to 6). Incorporation of honey and EEP significantly affect the pH of formulation (p<0.05). In this study pH of drug loaded microemulsion (DM) was lower (acidic) than pH of blank microemulsion**.** pH of drug loaded microemulsions ranged from 4.86±0.057 to 5.2±0.1 (Table 3). This decrease in pH was might be due to acidic nature of honey and EEP. [24, 25, 26]

Conductivity study of microemulsion was performed to check the macrostructure of microemulsion and to determine the type of microemulsion. In this study conductivity of microemulsions was increased from F_4 to F_8 (Table 3). This was due to increase in water contents of formulations from F_4 to F_8 which was consistent with previous study in which great change in conductivity of microemulsions had occurred with increase of water contents. Statistical comparative study of blank and drug loaded microemulsions represented that all blank and drug loaded microemulsions were also significantly different from each other in term of conductivity**.**

Increase in conductivity of drug loaded microemulsion was might be due to hydrophilic nature of honey.[27, 28]

The mean viscosities of blank and drug loaded microemulsions have been given in Table 3 at 20, 50 and 100 rpm. Viscosities of microemulsions were increased from F_4 to F_8. This was due to increased in water contents of formulation from F_4 to F_8. In the presence of large amount of water hydrophilic chain of tween 20 (non ionic surfactants) was strongly hydrated, connected together with hydrogen bonds, allowed strong interactions among them hence causing increase in the viscosity of microemulsions from F_4 to F_8 (Greater amount of water and smaller amount of surfactants). Blank and drug loaded microemulsions were also significantly different from each other ($P<0.05$) in term of viscosity. Addition of honey and propolis decreased the viscosity of blank microemulsions. This was due to lipophilic nature of propolis and hydrophilic nature of honey. Because of lipophilic nature, propolis remained in oil phase but honey incorporated in the surfactant film preventing the formation of strong hydrogen bonds among non ionic surfactant and water. [28, 29, 30]

In this study average particle or droplet size of blank and drug loaded microemulsion was less than 200 nm. These droplet sizes of microemulsions were consistent with previous studies in which particles size of microemulsion ranged from 100 to 500 nm. This value was also found in close agreement with previous study according to which droplet size of microemulsion was ranged from 20 to 200 nm. Droplet size of drug loaded microemulsion was not significantly different ($p>0.05$) from blank microemulsion. [28]

Quercetin is a major flavonoid present in *nigella sativa* honey and propolis. Quercetin contents of DM_4, DM_7 and DM_8 microemulsions were 0.43 ug/ml, 47ug/ml and 1093ug/ml respectively**.** HPLC peaks of flavonoids contents of microemulsions have been shown in Figure 2. Flavonoids contents are highly soluble in DM_8 microemulsion followed by DM_7 microemulsion. This is because of increase in droplet size from DM_4 to DM_8 which was consistent with previous study in which drug contents of microemulsion increased with increased in droplet size. [8, 31, 32]

On the basis of results of stability study BM_4, BM_7, DM_4 and DM_7 microemulsions were rejected because phase separation occurred in them after the period of 45 days at 25^0C. Drug was also precipitated in drug loaded formulations. BM_8 and DM8 microemulsions were accepted because they were transparent having no sign of phase separation after the period of 45 days and drug was not precipitated in DM_8. This stability of DM_8 microemulsion was consistent with previous study in which microemulsion of Indian penny wort, walnut and turmeric plants extracts were evaluated for their stability over the period of 45 days and no visible change occurred in them.[23]

Results of antimicrobial activity indicated that there was significant difference ($p<0.05$) between zones of inhibitions of Honey, EEP, SSD cream, BM_8 and DM_8. ZI of DM_8 was greater than ZI of honey and EEP against staphylococcus aureus (Table 4). This was due to synergistic effect of honey and EEP which increased the ZI of DM_8. Synergistic effect of honey and EEP was due to presence of flavonoids and phenolic contents in them and stimulation of antibody production mechanism. Zone of inhibition of all the products has been shown in Figure 3.[2, 9, 33, 34]

Table 4: Mean zones of inhibition (mm) against staphylococcus aureus

Samples	Zone of inhibition (ZI) Mean ± SD mm
Nigella sativa honey	11.65±0.41
EEP	21.46±0.451
Drug loaded microemulsion (DM_8)	26±1
Blank microemulsion (BM_8)	15.67± 1.53
SSD	18.53± 0.4

Figure 3: Visualization of zone of inhibition against staphylococcus of DM_8(Drug loaded microemulsion), BM_8(Blank microemulsion), H (Honey), concentrated EEP (Ethanol extract of propolis) and SSD (Silver sulphadiazine) cream.

Table 5: Percentage wound contraction of albino rats

Treatment Group	Percentage wound contraction (Mean ± SD)				
	3rd	7th	10th	14th	20th
Control	5.43± 2.59	16.72± 3.39	33.50± 8.01	50.73± 7.94	78.99± 3.37
BM_8	16.32± 1.53	34.64± 3.41	49.16± 4.75	66.85± 5.1	81.83± 2.35
DM_8	33.37 ±3.57	49.44±3.28	70.46±6.57	89.76± 2.85	99.31± 0.51
SSD Cream	28.78± 3.83	35.89± 1.89	51.63± 5.25	73.94± 5.33	89.07± 2.28

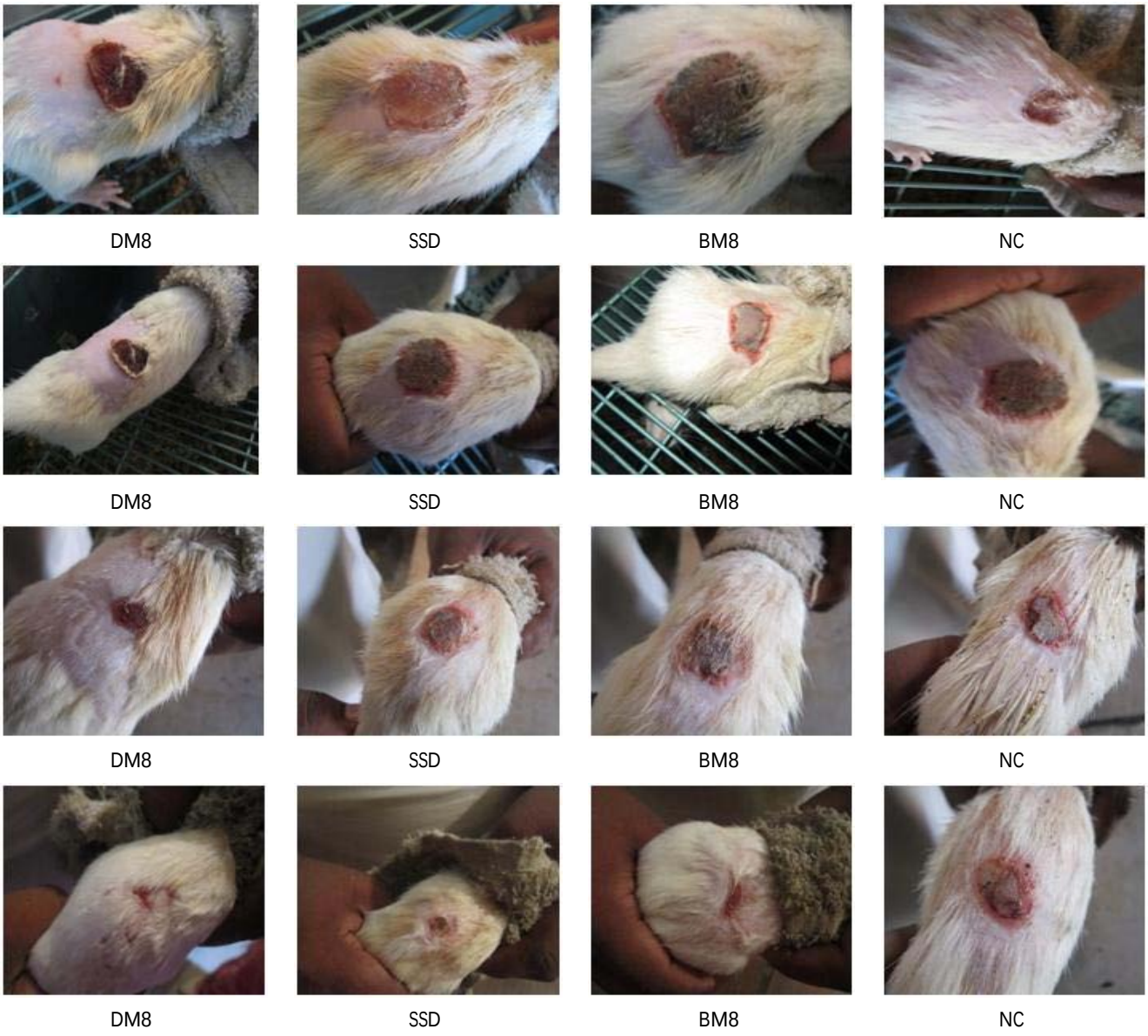


Figure 4: Percentage wound contraction on 7th, 10th, 14th and 20th day respectively, DM8: Drug loaded formulation, BM8: Blank microemulsion, SSD: Silver sulphadiazine cream (Positive control), NC: Negative control.

***In-vivo* studies**

In the present study percentage wound contraction in all four groups was calculated by measuring the wound size on 3rd, 7th, 10th, 14th and 20th day (Table 5). Percentage wound contraction produced by DM_8 on 20th day was 99.305± 0.5 which was greater than percentage wound contractions produced by other three treatments. Percentage wound contractions produced by these four treatments were significantly different (p<0.05) from each other on 7th, 10th, 14th and 20th day. This pattern of wound size reduction in entire treatment groups had been shown in figure 4.

In present study faster rate of burn healing of DM_8 was due to antimicrobial action of honey and EEP. Previous studies have reported that antibacterial activity and burn healing potential of honey was due to presence of hydrogen peroxide, low pH, osmotic pressure, lymphocytic and phagocytic action and presence of phenol and flavonoids contents. Osmotic environment of honey left very few free water molecules which prevented the growth of microorganisms. Low pH of honey and propolis also inhibited the growth of microorganisms. The fast burn healing activity of microemulsion was also due to EEP which was present in this formulation. Many studies also described the anti-inflammatory activity of EEP. According to them propolis reduced the edema and allergic reaction. Flavonoids contents of propolis boost immunity and white blood cell. All these factors promote the burn healing potential of DM_8 and it showed significantly different (p <0.05) effects from silver sulphadiazine cream.[3, 6, 7, 24, 35]

CONCLUSION

Microemulsion of honey and EEP was formulated successfully. It had greater antibacterial and burn healing potential than honey or EEP. It might be due to synergistic effect of honey and EEP, greater penetration of drugs in

the skin due to presence of surfactant and co surfactant in microemulsion which increased the membrane permeability of both active ingredients (Honey and EEP). All these factors promoted the burn healing potential of microemulsion and it showed statistically significant effects than SSD cream.

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