



## Research Article

**Evaluation the Effect of *Melaleuca Alternifolia* (tea tree) oil as a New Topical Therapy in the Treatment of Burn**TAREK A AHMED<sup>1</sup>, BASHER E ABD ELAZIZ<sup>2</sup>, MAMDOUH M ELMOEMEN<sup>2</sup>, ABD ELMONIEM H HOTAH<sup>3</sup><sup>1</sup> Department of Pharmaceutics and Industrial Pharmacy, Faculty of Pharmacy, Al-Azhar University, Cairo, EGYPT<sup>2</sup> General Surgery Department, Faculty of Medicine- Al-Azhar University, Faculty of Medicine, Al-Azhar University, Cairo, EGYPT<sup>3</sup> Plastic Surgery Department, Faculty of Medicine- Al-Azhar University, Faculty of Medicine, Al-Azhar University, Cairo, EGYPT**ARTICLE DETAILS***Article history:*

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**ABSTRACT**

The rationale behind this study was to develop a topical tea tree oil formulation and to evaluate its usefulness as a new therapy in the treatment of burns. *Melaleuca alternifolia* (tea tree) oil 5% cream was prepared, characterized, and compared to silver sulphadiazine (SSD) 1% which is the most frequently used topical therapy as regard the pain, infection, healing and epithelization. The healing was achieved in 90% of patients of study group within two weeks, in comparison to 80% of patients of control group. No local irritation of skin was reported in study group but two patients were reported in control group. *Melaleuca alternifolia* (tea tree) oil topical formulation showed an apparent anti-inflammatory effect, reduce edema and erythema that occurs after burn, and showed analgesic effect by relief the pain shortly after use, so the patient would not need further analgesic treatment as those under treatment with SSD cream.

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**INTRODUCTION**

Topical delivery of drugs has been recognized as an alternative route to oral therapy. The primary advantage of topical administration is the direct accessibility of the drug to the affected tissues with minimal systemic side effects [1]. The therapeutic efficacy of a topical formulation depends on both its composition and the physicochemical properties of the penetrant. The vehicle composition can affect drug release and skin permeability properties [2, 3]. Therefore, the selection of an appropriate vehicle is one of the most important guidelines in increasing the efficacy of a topically applied drug [4, 5].

Australian native plant *Melaleuca alternifolia* (Tea Tree) oil has recently emerged as an effective topical antimicrobial agent active against a wide range of organisms. Tea tree oil is reported to have antibacterial, antifungal, antiviral, anti-inflammatory and analgesic properties. Currently, tea tree oil is used in cosmetics, healthcare and antiseptic products [6].

*Melaleuca alternifolia* (tea tree) oil is essential oil, comprised of terpene hydrocarbons mainly monoterpenes, sesquiterpenes, and their associated alcohols. Terpenes are volatile aromatic hydrocarbons and may be considered polymers of isoprene. The TTO report approximately 100 components on their range of concentrations and its composition is regulated by an international Organization for Standardization standard as (ISO4730). The activity of TTO is attributed mainly to terpinen-4-ol, a major component of the oil.

The mechanism of action of TTO against bacteria is through disruption of biological membranes and their vital functions [7]. Lysis and the loss of membrane integrity and function manifested by leakage of ions and inhibition of respiration were demonstrated after TTO treatment [8].

The aim of the present work is to evaluate the effect of *Melaleuca alternifolia* (tea tree) oil 5% as a new topical therapy in the treatment of burn wound compared to silver sulphadiazine 1% which is the most frequently used topical therapy as regard the pain, infection, healing and epithelization.

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## **MATERIALS AND METHODS**

### **Materials**

Liquid paraffin from El-Nasr Pharmaceutical Chemicals Co. (Cairo, Egypt). Cetyl alcohol, white wax, and sodium borate, from Fisher Scientific (Pittsburg, PA). Tea tree oil from Ord River tea tree oil plantation company (Australia)

### **Methods**

#### ***Preparation of tea tree oil 5% w/o cream***

TTO was mixed with cetyl alcohol, white wax, and mineral oil. The mixture was melted at 60 °C. The calculated amount of sodium borate was dissolved in the distilled water. The aqueous part was warmed to about the same temperature of the melted oil phase and then added gradually with continuous stirring until W/O emulsion has been formed.

#### ***Evaluation of TTO Pharmaceutical Topical formulations***

##### ***Organoleptic Characters***

The prepared plain and medicated creams were tested for their color, odor, texture, phase separation or bleeding as well as the feel on application (stiffness, grittiness, greasiness) once the preparation is applied on the skin and also after two minutes of application.

##### ***Homogeneity Test***

A small quantity of the prepared cream was pressed between the thumb and index finger and the consistency of the base is noticed (whether homogeneous or not) and if there is any coarse particles appeared or detached on fingers. Also, the homogeneity was detected when a small quantity of the base is rubbed on the skin of the back of the hand.

##### ***Rheological Properties of Semisolid Preparations***

Brookfield LVT-D V-II programmable viscometer of Engineering Laboratories, Inc. (Middleboro, MA) was connected to a thermostatic water bath adjusted at 25 °C. The viscosity of the prepared plain and medicated cream was determined.

The viscosity measurement was done with spindle 40. About 0.5 g of the preparation was placed inside the plate and carefully closed. The experiment was performed by increasing the spindle speed gradually. As the speed was increased, torque also increased. The data obtained in the torque range of 10-90% were taken. Thirty seconds were left between each two successive speeds. Once the torque reached 90%, the speed was reduced gradually, with the

same order as the increasing one, until a torque of 10% was found.

Rheological parameters including shearing stress, rate of shear, viscosity, and yield value were directly obtained from program. Complete rheograms was obtained by plotting the rate of shear as a function of the shearing stress. The areas of the hysteresis loops between the upward (right side) curves and the downward (left side) curves in the rheograms of both plain and medicated bases were determined by cut and weight method using tressing paper, the rheogram and the rheological parameters were studied and evaluated to be in good agreement with Tarek et al 2010 [9].

#### ***Therapeutic evaluation of the prepared TTO Topical preparation***

The patients included in this study were among those patients attending the emergency unit of Banha teaching hospital, ministry of public health. They were categorized into two groups, the control group included (20) patients treated locally with Silver Sulfadiazine (SSD) cream 1%, and the study group included (20) patients treated locally with tea tree oil (TTO) cream 5%. Of these (17) were male children's, (15) female children's, (4) adult male, and (4) adult female.

Immediately after attending of the patient in the hospital, the patient was taken to a clean room in which a complete patient history was taken regarding, the events of injury, time, location (open or closed space), and cause of burn injury.

##### ***I) Examination***

A: The patient clothing was removed for initial examination of burn wound and thorough physical examination, to detect any associated major injury.

B: Initial examination of burn wound involved estimation of the extent, depth and distribution of burn injury for treatment purposes and to determine whether inpatient or outpatient care is required.

##### ***II) Management of burn wound***

When the patient came to the hospital, signed consent was obtained from all patients participating in this study regarding the use of TTO cream as a local treatment for burn wound, and explaining the aim and methods of treatment.

- 1) To minimize further contamination, all patients were taken to a clean room where aseptic technique was followed. All personnel who came in contact with the patient used surgical masks, gowns and gloves.
- 2) The patients wound cleaned with saline solution.
- 3) Loose tissue and blisters were debrided.
- 4) The dressing was done each other day for burn wounds and consists of topical cream applied directly to the wound surface, then wrapped in several layers of gauze.

### III. Laboratory part

The burned patients were subjected to routine laboratory investigations, during the course of this study, at first, third, seven and 15 postburn day.

- 1) Blood picture; hemoglobin per cent, haematocrit value, red cell count, total and differential leucocytic count.
- 2) Culture of burn wounds; were done on agar medium aiming to isolation and identification of the sensitivity of the infected organism to the antibiotic.

Systemic antibiotic was used for the patients that show signs and symptoms of local infection, according culture and sensitivity for burn wound as showed by copious wound discharge, rapid eschar separation, conversion of superficial partial thickness into deeper degree, erythema of surrounding tissues and persistence of local pain. Also systemic antibiotic introduced in suspected septicemic microbial invasion as hyper or hypothermia chills, hypotension, paralytic ileus and confusion or delirium and laboratory finding of rapid rise or fall in white cell count and anemia.

The patients were classified into two groups; the first group: the control group that treated with Silver sulfadiazine cream and the second group: for patients treated with Tea tree oil cream.

## RESULTS AND DISCUSSION

### Preparation of tea tree oil 5% w/o cream

Semisolid topical preparations include; creams, ointments, and gel bases. As an oil, TTO is difficult to formulate in gel bases or water soluble ointment base since, these bases are hydrophilic while the oil is hydrophobic and so it will be more appropriate to formulate in a w/o base to increase the diffusion coefficient and hence the release of hydrophobic drug in lipophilic base [1].

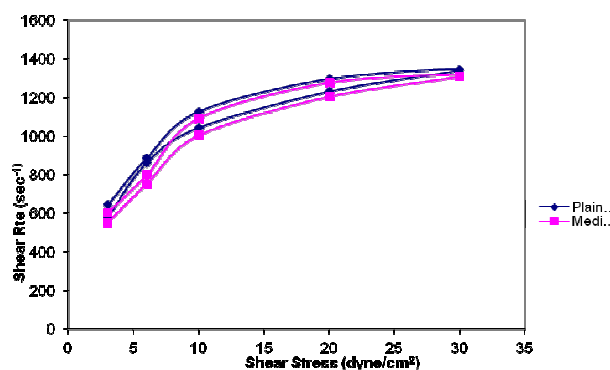
Our experience with topical preparations showed that, the drug especially the anti-inflammatory concentration in the topical formulation is ranged between one and 10% [9]. The concentration of TTO in this study was chosen to be in the medium concentration (5%).

### Characterization of the organoleptic character and homogeneity test

According to the physical investigation of the tested bases, the organoleptic characters of the stated bases showed good texture, homogeneity and ease of spreading.

### Rheological Properties of Semisolid Preparations

The rheological property determination for the prepared creams within the experimental conditions tested was shown in Fig. 1 for both plain and medicated bases. The figures represent the relation between the shearing stress and the shearing rate.



**Figure 1:** Relation between shear rate and shear stress of W/O ointment

It was clear that, the plain and medicated creams exhibited a plastic flow with thixotropic behavior. The yield values and the hysteresis areas of the above bases were calculated as shown in Table 1.

**Table 1:** The Values of Viscosities, Thixotropic behavior and Yield Values of Plain W/O base and medicated base containing 5% Tea tree oil

Formula	Max. Viscosity (cp.)	Min. Viscosity (cp.)	Thixotropic behavior (cm <sup>2</sup> )	Yield Value (dyne/cm <sup>2</sup> )
Plain W/O	3980	865	1.735	423
Medicated W/O	3764	799	1.710	416

### Therapeutic evaluation of the prepared TTO Topical preparation

Tea tree oil is reported to have an antiseptic action [10], antifungal action [11, 12], and antiviral effect [13, 14], the oil is also reported to prevent oxidative damage and the activation of other cells in more chronic inflammatory states [15]. Study, in which 217 patients from a dermatology clinic were patch tested with 10% TTO, found no irritant reactions [16].

The patients in this study have thermal burn injuries of different areas of the body except the face, different extents (less than or equal to 10%). The results of test of significance were put in the Table 2, minor burns generally treated on an

outpatient basis, comprise the majority of thermally injured patients. The pain of superficial 2nd degree burn causes agony for burned patients. So the patients of both groups were given analgesic treatment in the first 24h to relieve the pain and prevent the neurogenic shock, no more analgesic was required for Melaleuca alternifolia group patients due to its analgesic effect, the SSD group patients were given mild analgesic treatment before each dressing to relieve the pain that occurs after the dressings, due to its irritant effect of SSD cream. The difference was significant between both groups as regard the pain.

**Table 2:** Comparison between SSD group and TTO group as regards

Clinical data	SSD group (n=20)	TTO group (n=20)	p
Age			
2-10y	15	13	
11-20y	1	3	>0.05
21-40y	4	4	
Sex			
Male (21)	11	10	>0.05
Female (19)	9	10	
Burn %			
2% (2)	1	1	
3% (24)	12	12	
4% (8)	4	4	>0.05
5% (4)	2	2	
10%(2)	1	1	
Site of burn			
Upper limb(16)	8	8	
Lower limb(18)	9	9	
Trunk (2)	1	1	>0.05
Trunk+thigh(2)	1	1	
Trunk+buttock+ thigh(2)	1	1	

P<0.05= significant; P >0.05= not significant

**Table 3 :** Comparison between SSD group and TTO group as regard

Clinical data	SSD	TTO	P
pain	0	20	<0.05
Wound discharge	9	3	<0.05
Local irritation	2	0	>0.05
Healing time	16 patient in 15 days 4 patient after 15 days	18 patient in 15 days 2 patient after 15 days	>0.05 >0.05
Further treatment			
Antihistaminics	2	0	>0.05
Analgesics	20	0	<0.05

P<0.05= significant; P >0.05= not significant

The healing was achieved in 90% of patients of study group within 2 weeks in comparison to 80% of patients of control group, the comparison between the two groups were significant as listed in Table 3.

No local irritation of skin was reported in study group but two patients were reported in control group. The Local signs of infection were found in

nine patients of control group. In comparison, infection was found in only three patients of study group and so, there is a significant difference between both groups regarding infection. The progresses of the cure and patients compliance were obvious, photo taken and illustrated in pictures (1-4).



**Picture 1:** The upper limbs of TTO group at day 3 (A) and day 15 (B) for Patient number (2).



**Picture 2:** The upper limbs of SSD group at day 1 (A) and day 15 (B) for Patient number (2).



**Picture 3:** The lower limbs of TTO group at day 1 (A), day 3 (B), day 7 (C), and day 15 (D) for Patient number (3).



**Picture 4:** The lower limbs of SSD group at day 3 (A), day 7 (B), and day 15 (C) for Patient number (3).

**Table 4a:** Comparison of the Results of routine laboratory investigations of SSD group and TTO group, 24 hours post burns

	Group	N	Mean	Std. Deviation	t	p
HB	SSD	20	12.7355	1.31933	0.8	>0.05
	TTO	20	13.0885	1.59636		
RBCS	SSD	20	4194.8000	472.81137	0.8	>0.05
	TTO	20	4332.2000	648.66694		
PCV	SSD	20	38.4500	3.99309	0.8	>0.05
	TTO	20	39.5500	4.74036		
Platelet	SSD	20	332.5500	59.21013	0.7	>0.05
	TTO	20	343.9000	49.08414		
TLC	SSD	20	6673.2000	1448.99248	1.3	>0.05
	TTO	20	6221.5500	677.31299		
B	SSD	20	18.4500	40.88041	0.4	>0.05
	TTO	20	22.6000	41.63551		
E	SSD	20	219.8500	22.54884	1.7	>0.05
	TTO	20	234.2000	30.05714		
N	SSD	20	2094.1000	465.20475	4.3	<0.05
	TTO	20	2775.5500	544.82460		
I	SSD	20	4405.0000	1080.06028	1.9	>0.05
	TTO	20	3850.8500	750.07314		
M	SSD	20	261.6500	140.58123	0.2	>0.05
	TTO	20	253.2500	111.33443		

P<0.05= significant; P >0.05= not significant

**Table 4b:** Comparison of the Results of routine laboratory investigations of SSD group and TTO group 15 day post burns

	Group	N	Mean	Std. Deviation	t	p
HB	SSD	20	12.7355	1.31933	0.8	>0.05
	TTO	20	13.0885	1.59636		
RBCS	SSD	20	4194.8000	472.81137	0.8	>0.05
	TTO	20	4332.5000	648.60884		
PCV	SSD	20	38.4500	3.99309	0.8	>0.05
	TTO	20	39.5500	4.74036		
Platelet	SSD	20	332.5500	59.21013	0.7	>0.05
	TTO	20	343.9000	49.08414		
TLC	SSD	20	5873.6000	1007.91496	0.1	>0.05
	TTO	20	5845.4000	768.77787		
B	SSD	20	12.4000	26.80613	1.5	>0.05
	TTO	20	2.8000	7.28806		
E	SSD	20	219.8500	22.54884	2.7	<0.05
	TTO	20	204.9500	9.82732		
N	SSD	20	2422.9000	476.05273	3.6	<0.05
	TTO	20	2975.9500	502.95029		
I	SSD	20	3882.4500	683.77401	0.2	>0.05
	TTO	20	3850.3500	521.27175		
M	SSD	20	261.6500	140.58123	0.3	>0.05
	TTO	20	250.9000	113.40653		

P<0.05= significant; P >0.05= not significant



From the data presented in Tables (4a and 4b) showing the results of blood picture analysis, it was also clear that there was a significant progress in the cure of the tea tree oil treated group as compared to the control group.

Systemic antibiotic was used for the patient that shows signs and symptoms of local infection, according culture and sensitivity for burn wound.

The results of the present work are in agreement with that of Dryden et al 2004 [10] who reported more efficacy of *Melaleuca alternifolia* (tea tree) oil than SSD for open skin lesions. Moreover the antimicrobial effect of *Melaleuca alternifolia* oil was explained by Carson, et al 2006 [17] who report the susceptibility of broad range of organisms for *Melaleuca alternifolia* oil, in both vivo and in vitro. Healing was evaluated by clinical assessment. The healing and epithelialization occur in 18 patients (90%) within two weeks and in two patients (10%) after 15 days in the study group, compared to healing in 16 patients (80%) within two weeks and in four patients (20%), after 15 days in the control group. Irritation occurred for two patients in controlled group in the form of local erythema and itching and the patients were treated with antihistamines and did not need to discontinuation of therapy. There is a significant difference between both groups regarding local irritation. The results of the present work are in agreement with that of Veien, et al 2004 [16], who reported no irritant reactions to *Melaleuca alternifolia* (tea tree) oil. We did compare our new formulation to the most popular and widely used marketed product, and that is why we chose SSD cream 1% in a comparative study, it is important here to mention that, no one of the authors have any direct financial relation with this product.

### Conclusion

The results of the present work, clearly showed that *Melaleuca alternifolia* (tea tree) oil cream 5% would be suitable and effective as local antimicrobial agent for minor burn injuries, it is not irritant and accelerate the healing process of burn wound in comparison to SSD cream 1%,

and could be used as antiseptic for open lesions wound. For more extensive burns, more studies are needed.

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