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BALANITES KERNEL OIL FOR THE TREATMENT OF DERMATOPHYTES: A CLINICAL TRIAL

Abdalla Mohamed Toum[1], Nour Ahmed Osman[2], Elnour Elamin Abdelrahman [2], Ismail Hassan Hussein[3] and SalahAhmed Elhussein[3, 4]

1- Faculty of Medicine, University of Gezira, Wad Medani, Sudan.(e.mail : drabdaltoum@yahoo.com)
2- Biotechnology Centre, Faculty of Engineering and Technology, University of Gezira, Wad Medani, Sudan.
3- National Oilseed Processing Research Institute, University of Gezira, Wad medani, Sudan.
4- correspondance : e-mail: elhusseinsalah@hotmal

Abbreviations: BKO = Balanites kernel oil, T.= tinea, S.D. = Sudanese dinars.

ABSTRACT

In a previous in vitro study, we have shown that the kernel oil of fruits of the tree Balanites aegyptiaca referred to as Balanites kernel oil ((BKO) is active against dermatophytes (i.e. superficial mycosis, ringworms, tineas (T. captitis, T. cercinata and T. pedis). We report here our clinical trials with BKO. Trials were performed on patients presenting at Wad Medani Dermatology Teaching Hospital as well as primary school children in Elsoreeba Town (5 km south of Wad Medani). Not all patients followed treatment till completely cured. Patients treated with BKO (half of the total) achieved complete cure in 3-5 weeks, on average, while those treated with the standard antifungal drug Miconazole (half of the total patients) did the same in the longer period of 3-8 weeks. Photographs showing progress of response to BKO treatments are included. BKO has great potential for development as a commercial drug for the treatment of dermatophytes.

INTRODUCTION

Dermatophytes are superficial fungal infections which affect the outer layer of the skin, the nail and the hair. They are fungi that require keratin for growth and they spread by direct contact from other people (anthropophilic), animals (zoophilic) or soil (geophilic organisms). Many species of these infectuous fungi, recognized by the nature of macro conidia (asexual spores), belong to the three genera, Trichophyton, Microsporum and Epidermophyton (Rook et al. 1988) [(1)]. Species of Trichophyton affect the skin, hair and nail, those of Microsporum affect the skin and hair while species of Epidermophyton affect the skin and nail. There are

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many species; their spores can live for more than a year in human skin scales in the environment. Dermatophtes are referred to as "tinea" infections and they are also named after the body site involved (Hunter, 1995) [2]. Skin diseases are widespread in different areas of Sudan and the history of dermatology in Sudan has been reviewed by Ahmed (2004) [3]. The most widely spread superfical mycoses causing species in Sudan are Trichophyton soudanense, T. rubrum, T. schoenleinii, T. violaceum and T. audouinii. The major diseases are Tinea capitis, Tinea pedis, Tinea corporis, Tinea ungum and Tinea cruris. Tinea capitis is especially prevalent among school children and it is characterized by irregular alopecia and scaling. Generally Tinea capitis can be identified by the presence of branching hyphae and spores on potassium hydroxide (KOH) microscopy, but if spores or hyphae are not visualized, cultures of samples from, affected areas can be used to detect specific disease-causing fungi. Also, wood's lamp may help detection of certain species through its fluorescence (Hainer, 2003) [4].

The major cause of Tinea capitis today is Trichophyton tonsurans (AbdelRahman, 1997 [5], Aly, 1999)[6], Table 1 shows the topical therapy used to treat superficial mycoses (Evans et al., 1997 [7] . Friedlander, 2000) [8]. Only the major chemical groups of drug's are mentioned.

Table 1: Current topical therapy for dermatophytes infection

Agent groups	Formulation	Frequency of application
Allyamines	1% cream, gel or solution	Once or twice daily
Benzylamines	1% cream	Once or twice daily
Imidazoles	1% cream, solution or lotion 1% shampoo 2% cream, spray, powder	Twice daily Once daily Twice daily

Balanites kernels, roasted and pounded, are traditionally used in a few areas in Western Sudan, according to Sudanese folk medicinal beliefs, to treat a variety of skin disease (Osman, 2001) [9]. Our previous in vitro work (Osman et al., 2006) [10] has pointed to the great prospect of the oil of Balanites agyptiaca as a potential antifungal agent against Miccrosporum audouinii, Trichophyton soudanense and T. mentagrophytes causing the diseases mentioned above. We report here our findings on clinical trails performed with this oil.

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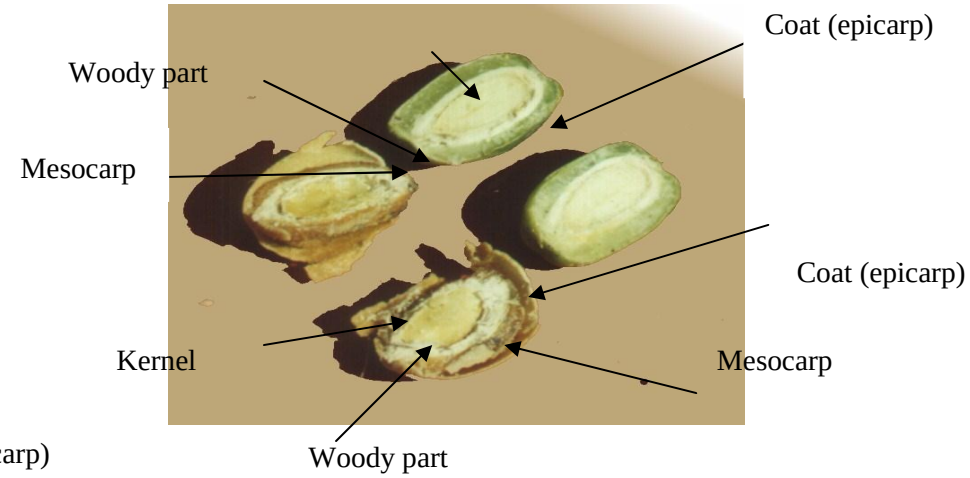
Specific objectives of this study included determining the effective dose and to extend our in vitro work on BKO to clinical trails. A major impact of this work, if Balanites oil proved to be an effective antifungal agent, at the clinical level, is reduction of treatment cost. A well formulated Balanites oil-based drug may find international demand.

MATERIALS AND METHODS

Preparation of Balanites oil:

All solvents used were of standard analytical grade. The oil was prepared from the separated fruit kernel (Fig. 1) by Soxhlet extraction using hexane according to the American Oil Chemists Society (AOCS) methods (1973) [11]. The solvent was completely removed in a rotary evaporator. The crude dried oil was packed in 20 ml screw-capped ampoules for dispensing to patients.



(a)

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(b)

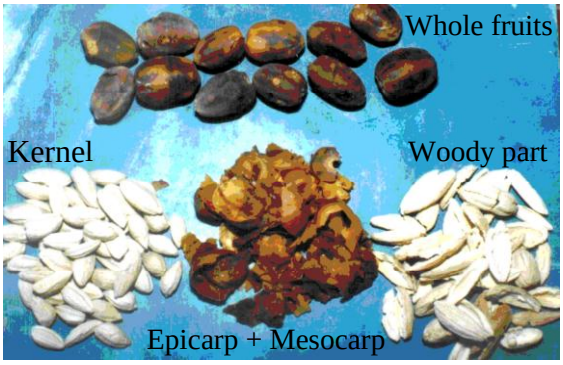

Fig. 1 (a & b): The Balanites fruit (Laloab) and its parts.

Clinical test

Our targets were patients presenting to Wad Medani Dermatology Teaching Hospital, referred from rural hospitals and health Centres. They were of different age groups of both sexes. Also targeted were pupils (girls and boys) of Elsoreeba Primary School. The school, 5 km south of Wad Medani, was regularly visited. In-form consent was obtained from all selected patients before their entry in this study (Fig. 2). The diagnosis of each patient was done first clinically and then confirmed by the University of Gezira Medical Laboratory, Wad Medani, Sudan, before starting medical treatment. The diagnostic test involved taking scrapings from the edges of affected areas, adding potassium hydroxide and examining microscopically for spores and hyphae. All patients were photographed before, during and after treatment which was done once a week till complete cure was achieved. The latter was confirmed by laboratory findings. Each patient had a follow-up form (Fig. 2). All of the case group pateints received either BKO or Miconazole therapy, the standard anti-fungal drug (pateints were initially assigned to either the test or control group by random selection. Thereafter, the patient remained in the group assigned)

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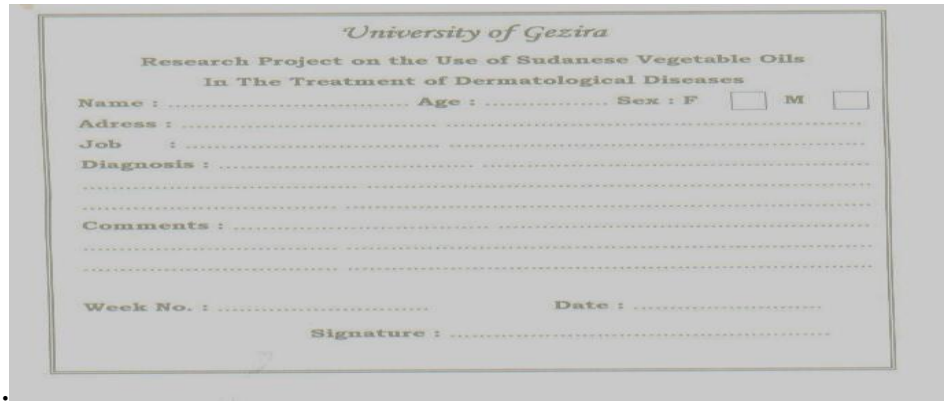
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Research Project on the Use of Sudanese Vegetable Oils
In The Treatment of Dermatological Diseases

Name : ..... Age : ..... Sex : F ☐ M ☐

Adress : .....

Job : .....

Diagnosis : .....

.....

.....

Comments : .....

.....

.....

Week No. : ..... Date : .....

Signature : .....

Fig. 2 : Sample form used for patient's data and signature (consent)

RESULTS AND DISCUSSION

Table 2 shows the overall breakdown of patients involved in this study. Eightyfive patients started the treatment (BKO or Miconazole-Mic-), thirty-four of them discontinued treatment after two weeks because of long distance, transport problems and socioeconomic reasons. Nineteen patients showed considerable improvement after 2-4 weeks of treatment. However, presumably for the same reasons, they discontinued treatment (Fig. 4). Thirty-two patients continued the treatment to the end, i.e. till totally cured (Fig. 3), sixteen of them were under BKO treatment and the other sixteen received Miconazole. All patients (case and control groups) affected by Tinea capitis showed the presence of branching hyphae and spores under laboratory examination (KOH microscopy). Complete cure, at the end of treatment, was similarly confirmed.

The shorter time for complete cure was observed in patients treated with BKO (25 weeks), whereas those treated with Miconazole took a longer period of time (3-8 weeks).

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Table 2: Breakdown of patients of the study: their numbers, diagnosis, treatment received and their cure rates (Mic=Miconazole).

Type of patients	Number of patients		Diagnosis		Comments on response to treatment
	Case (BKO)	Control (Mic)	Clinical	Laboratory (hyphae & spores)	
Group 1	18	16	+ve	+ve	Patients received one or two treatments (1-2 weeks) but did not show up again
Group 2	8	11	+ve	+ve	Patients markedly improved but discontinued treatment (2-4 weeks)
Group 3	16	-	+ve	+ve	Continued treatment till totally cured, in 2-5 weeks
Group 4	-	16	+ve	+ve	Continued treamtment till totally cured, in 3-8 weeks

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Fig. 3a: Case no.1, Age: 5 years, Diagnosis: T. capitis, Treatment duration: 3 weeks

1 2 3 4 5

Fig. 3b: Case No.2, Age: 11 years, Diagnosis: T. capitis, Treatment duration:5 weeks

1 2 3 4 5

Fig. 3c: Case No.3, Age: 19 years, Diagnosis: T. capitis, Treatment duration: 5 weeks

1 3 4

Fig.3d: Case No: 4, Age: one year, Diagnosis: T. circinata, Treatment duration:4 weeks

1 2 3 4 5

Fig. 3e: Case No: 5, Age: 14 years, Diagnosis: T. capitis, Treatment duration: 5 weeks

1 2

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Fig. 3 f: Case no.6, Age: 8 year, Diagnosis: T. capitis, Treatment duration: 2 weeks

Fig. 3(a-f): Photographs of patients showing progress of treatment with BKO till complete cure (Group 3, in Table 2). Inserted numbers refer to the progress of treatment, in weeks. The last picture (photograph) in each case represents the state diagnosed as completely cured (Note that hair regrowth had just started in Fig. 3b and 3 c, at the end of BKO treatment).

Fig. 3 shows pthotographs of selected patients who continued treatment with BKO till completely cured (Group 3, Table 2). Fig. 4 contains photographs of some of Group 2 (Table 2) patients, i.e., those who markedly improved but discontinued treatment.

Hainer (2003) [4] reported on the difficulties of the therapeutic treatment of Tinea capitis. According to this author topical treatment is not effective and there is a need for a systemic antifungal agent that is able to penetrate the hair follicles. Moreover, with resistant organisms, treatment must be continued for 6 to 12 weeks. Griseofulvin was the only agent labeled for the treatment of Tinea capitis by the U.S. Food and Drug Adminstration at that time (Elewski, 2000 [12] . Hainer, 2003) [4] . In our study T. capitis was completely cured with externally applied BKO, without the need for a systemic drug.

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Fig. 4 a: Case No 1: Age: 6 year, Diagnosis: T. circinata, Treatment duration: 3 weeks

Fig. 4 b: Case No 3: Age: 5 year, Diagnosis: T. capitis, Treatment duration: 2 weeks

Fig. 4 c: Case No4: Age: 20 year, Diagnosis: T. capitis, Treatment duration: 4 weeks

Fig. 4 (a-c): Photographs of patients who markedly improved with BKO but discontinued treatment (group 2, in Table 2).

The cost of Miconazole therapy treatment is currently estimated at 2000 S.D. per week (treatment up to 8 weeks), totalling up to 16000 S.D. for the full cost of treatment. On the other hand, we estimate that the total cost of BKO treatment is below 500 S.D. Moreover decreasing treatment duration has the economic impact of time saving.

Our research is continuing on to determine the exact nature of the active ingredient, its stability, the effective dose and other research work needed so as to proceed to the next stage of drug formulation. A properly formulated drug may find regional or international markets.

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