academicJournals

Vol. 11(4), pp. 37-41, July 2017
DOI: 10.5897/AJPAC2017.0717
Article Number: BB55B2F65311
ISSN 1996-0840

http://www.academicjournals.org/AJPAC

African Journal of Pure and Applied Chemistry

Full Length Research Paper

Comparative evaluation of the antipsoriatic activity of *Acalypha wilkesiana, Culcasia scandens* with *Kigelia africana* using the mouse tail model

Folashade Olatunbosun Oyedeji[1]* and Olufunso Samuel Bankole-Ojo[2]

[1]Department of Chemistry, University of Ibadan, Ibadan, Nigeria.
[2]Department of Physical Sciences, Wesley University, Ondo, Nigeria.

Received 31 January, 2017; Accepted 8 June, 2017

The mouse tail model was used to measure and compare antipsoriatic activity of *Acalypha wilkesiana* and *Culcasia scandens* with that of earlier reported *Kigelia africana* stem methanol extract by the same authors, with the objective of finding out which of these plant extracts can be a better drug option for the treatment of psoriasis. The results obtained showed that topically administered extracts (50-200 mg/ml) induced a significant and dose-dependent increase in %orthokeratosis in the epidermis of the mice tails. % orthokeratosis values were 35.5-43.4 (*A. wikesiana*), 29.7-47.4 (*K. africana*), 31.9-36.5 (*C. scandens*) for the methanol ointments; 29.3-36.2 (*A. wikesiana*), 32.3-58.2 (*K. africana*), 29.40-56.2 (*C. scandens*) for the hexane extracts. In general, the methanol extracts produced higher % othokeratosis. No deterioration in the general condition of the mice in any group was observed. However, erythema was observed on the tails of the mice on which the *K. africana* stem methanol extract ointment (200 mg/ml) was applied. No tail erythema was observed in any other group. Application of the ointments resulted in the softening of the tails. In general, the irritation potentials of the ointments were relatively low when compared to that induced by dithranol a drug commonly used in the treatment of psoriasis. Only the *A. wilkesiana* methanol extract ointment (200 mg/ml) showed greater than 40% drug activity. Thus, *A. wilkesiana* appears to be the better plant for use in possible drug development for the management and cure of psoriasis because *A. wilkesiana* ointment showed more prospects of being an antipsoriatic topical agent when compared to *C. scandens or K. africana,* as the drug activity of the methanol extract of this plant was greater than 40% and quite similar to that of *K. africana* without the corresponding irritation potential or erythema.

Key words: Psoriasis, mouse-tail model, *Acalypha wilkesiana*, *Culcasia scandens*, *Kigelia africana*, dithranol drug activity, irritation potential.

INTRODUCTION

Psoriasis is a chronic auto-immune skin disorder that affects 2% of the world population. The chronic, recurrent, psychological and complex nature of the disorder means that more efficient therapies are being sought (Singhal and Kansara, 2012; Dwarampudi et al., 2012; Suresh et al., 2013), in spite of the large number of treatment options available (Wong and Koo, 2012; Papp et al., 2012). In this study, we have scientifically and objectively assessed the effects of local plants used in the management and treatment of psoriasis in Nigeria

and some other countries in Africa using the mouse tail model.

Treatment of psoriasis often begins with topical treatments which involves the use of medications in creams or ointments that are applied to the skin and scalp. The challenges with the common topical agents include side effects like thinning of the skin, changes in skin colour, bruising and dilated blood vessels as those observed with the use of corticosteroids and the irritation caused by vitamin D analogues.

The importance of herbal remedies to the African Society includes the opportunity for cheaper treatment options, the presence of herbalist in the communities, and the use of herbs that are familiar and have always been used in those societies (Sambo, 2010; Kofi-Tsekpo, 2004; Elujoba et al., 2005; Mills et al., 2005; Oyeneye and Orubuloye, 1985).

The common herbs used in several parts of Nigeria for the treatment of Psoriasis and related diseases include *Acalypha wilkesiana, Kigelia africana syn. Kigelia pinnata and Culcasia scandens* (Fawehinmi et al., 2013; Haruna et al., 2013).

A. wilkesiana also known as Red Acalypha is locally and commonly used for the treatment of psoriasis especially in infants. A 50% aqueous ethanol extract of the plant revealed the presence of gallic acid, corilagin and geranin as compounds responsible for its antimicrobial activity (Alade and Irobi, 1993; Adesina et al., 2000).

K. africana also known as sausage tree or Worsboom is grown generally in the tropics. It has a wide variety of medicinal uses which includes the treatment of psoriasis (Olatunji and Atolani, 2009). Its varied medicinal properties may be due to the presence of numerous secondary metabolites. These compounds include irinoids, flavonoids, naphthoquinones and other volatile constituents (Sangita et al., 2009).

C. scandens is a climber that grows in the African tropical forests. It is used to treat psoriasis because of its strong anti-inflammatory and analgesic properties. The methanolic extract has been found to exhibit strong anti-inflammatory properties. Phytochemical analysis of the extract revealed the presence of reducing sugars, carbohydrates, alkaloids, glycosides, saponins, tannins, flavonoids and an unsaturated lactone ring of steroids (Okoli and Akah, 2000)

Cell proliferation is an important part of the pathogenesis of psoriasis. The mouse tail model is considered an adequate model for the study of the progress of this pathogenesis (Sebok et al., 2000; Singhal and Kansara, 2012; Schaper et al., 2013). In this model, the regular foci of parakeratosis, occurring in the adult mouse tail is used to study the ability of different topically delivered agents to produce orthokeratosis in these parakeratotic areas.

The antipsoriatic effect of *A. wilkesiana* and *C. scandens* as topical agents were evaluated using the modified albino mouse tail model (Bosman et al., 1992; Ledon et al., 2007) which had been used earlier to evaluate the effect of *K. africana* previously carried out in our lab (Oyedeji and Bankole-Ojo, 2012). The activity of *K. africana* reported was considered for comparative study and the data on the *K. africana* stem was used because of the high drug activity of this extract.

MATERIALS AND METHODS

Plant samples

Acalypha wilkesiana leaves and *C. scandens* leaves and stem were collected at the botanical garden of the University of Ibadan, Ibadan, Nigeria. All plant samples were subsequently identified by the Assistant Chief Plant Technologist and the officer-in-charge of the botanical garden. The plant samples were air dried and ground using an electric grinder. The *C. scandens* leaves and stem were ground together to form a composite sample.

Chemicals

Analytical grade methanol and hexane were used as solvents in the extraction process. Blue seal Vaseline was used as the vehicle for the plant extracts and as control.

Laboratory animals

The forty (40) male albino mice used for the study were purchased at Covenant farms, Iwo Road, Ibadan, Nigeria. The animals were then transferred to cages in the Experimental Animal Unit of the Faculty of Veterinary Medicine, University of Ibadan where they were kept and reared throughout the period of the study. They were sacrificed when they were 12 weeks and had an average weight of 10.53 g and an average normal length of 7 cm. The experiments were carried out in accordance with the ethical guidelines for investigations in laboratory animals [EE directive of 1886(86/609/EEC)].

Extraction process

Methanol and hexane extracts were obtained from the ground samples using a soxhlet extractor. The extracts were subsequently concentrated using a rotatory evaporator.

The modified mouse tail test

Ointments containing the plant extract and vehicle (Blue Seal Vaseline) were prepared to contain varying concentrations (200, 100 and 50 mg/ml) of the plant extract in the vehicle. 0.1 ml of the

*Corresponding author. Email: Omoeage2002@yahoo.com Tel: +234 7083572878.

Table 1. Percent orthokeratosis for tails treated with methanol and hexane ointments.

Plant extract	Methanol ointment concentration (mg/ml)	% Orthokeratosis	Hexane ointment concentration (mg/ml)	% Orthokeratosis
Acalypha wikesiana	50	35.5 ± 3.1	50	29.3 ± 2.7
	100	37.1 ± 2.3	100	35.5 ± 4.0
	200	43.4 ± 4.4	200	36.2 ± 2.1
Kigelia africana	50	29.7 ± 1.6	50	32.3 ± 3.6
	100	35.5 ± 1.7	100	50.1 ± 2.4
	200	47.4 ± 2.0	200	58.2 ± 1.62
Caulcasia scandens	50	31.9 ± 2.1	50	29.40 ± 3.2
	100	36.5 ± 2.4	100	56.2 ± 1.6
	200	35.7 ± 2.1	200	29.40 ± 3.2

Each measurement is a mean of triplicate values.

ointment was rubbed on the proximal parts of the tails of the mice. To ensure a good treatment contact time of 2 to 3 h, plastic cylinders were slipped over the tails of the animals to cover the treated portions and keep treatment in place. Tails treated with vehicle and tails left untreated were used as Controls 1 and 2, respectively. The animals were treated once daily in the morning hours for 2 weeks. Three animals were used per dosage group. At the end of the treatment, the animals were killed by cervical dislocation, the tails were cut-off and longitudinal sections of tails were prepared and stained with haematoxylin for histological examination (Ledon et al., 2007)

Histological examination

The presence of a granular layer or isolated granular layer cells induced in the previously parakeratotic skin areas were examined on 10 sequential scales of the albino mouse tail. Measurements were carried out at the border of the scales with a semi-automatic image evaluation unit.

Drug activity and percent orthokeratosis

The length of the granular layer (A) and the length of the scale (B) were measured to quantitatively evaluate the drug activity and percent orthokeratosis in those parts of the adult mouse tail, which normally have a parakeratotic differentiation. For each animal, 10 sequential scales were measured and the results given in % orthokeratosis per scale. Three animals were taken for one drug concentration or control group. Thus, 30 individual orthokeratosis values were obtained per test group. Per animal and per group mean and standard error of the mean were calculated.

$$\%\ Orthokeratosis = (A/B)\ x\ 100$$

$$\%\text{Drug activity} = \frac{Mean\ Ok\ of\ treated\ group - Mean\ OK\ of\ Control\ Group\ x\ 100}{100 - Mean\ OK\ of\ the\ control\ group}$$

OK = Orthokeratosis

Epidermal thickness

The distance between the dermo-epidermal borderline and the beginning of the horny layer was measured to obtain epidermal thickness. Five measurements per animal were made in every 10 scales and the mean of the different animals was calculated. The change in epidermal thickness was then calculated. The percentage change in the epidermal thickness is often regarded to be representative of the extent to which a substance causes irritation (Ledon et al., 2007).

$$\%\Delta\ Epidermal\ thickness = \frac{ET\ of\ \ treated\ group - ET\ of\ control\ group\ x100}{100 - ET\ of\ control\ group}$$

ET=Epidermal thickness

RESULTS AND DISCUSSION

The profiles of the percent orthokeratosis as shown on Table 1 indicate that the topically administered extracts induced a significant and dose-dependent increase in orthokeratosis in the epidermis of the mice tails. No deterioration in the general condition of the mice in any group was observed. However, erythema was observed on the tails of the mice on which the *K. africana* stem methanol extract ointment (200 mg/ml) was applied. No tail erythema was observed in any other group. Application of the ointments resulted in the softening of the tails. The induction of a granular layer by the topically administered plant extracts was measured in previously para-keratotic scale regions in the mice tails. In the tail skin samples of the control groups, lack of granular layer in the epidermal stratum was observed as expected. Epidermal thickness is regarded as a parameter indicating skin irritation. Thus, the larger the increase in epidermal thickness induced, the more likely the ointment is going to cause irritation on the human skin. In general, the irritation potentials of the ointments are relatively low when compared to dithranol (Agrawal et al., 2013) which is commonly used in treatment of psoriasis (Figures 1 and 2).

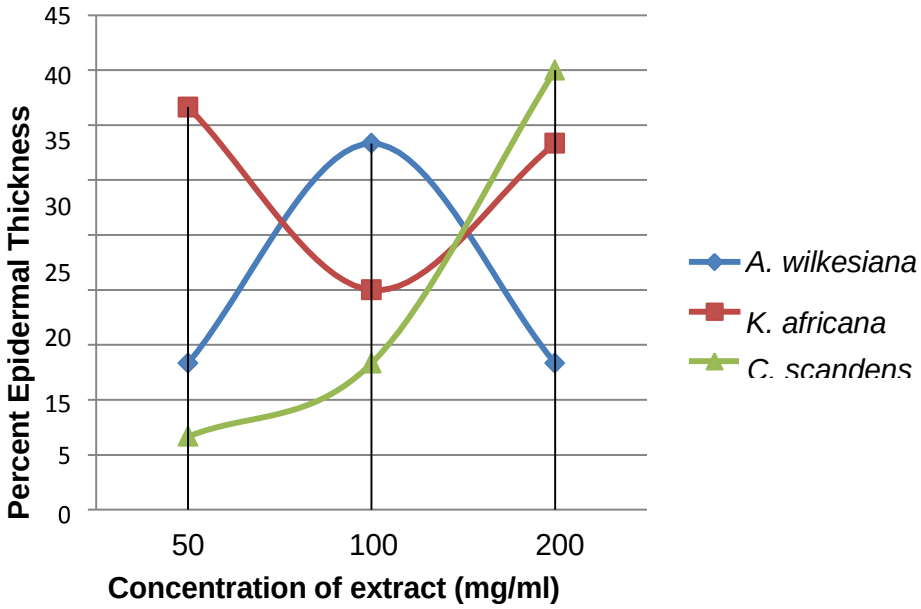

Figure 1. Change in percent epidermal thickness with concentration of methanol extract.

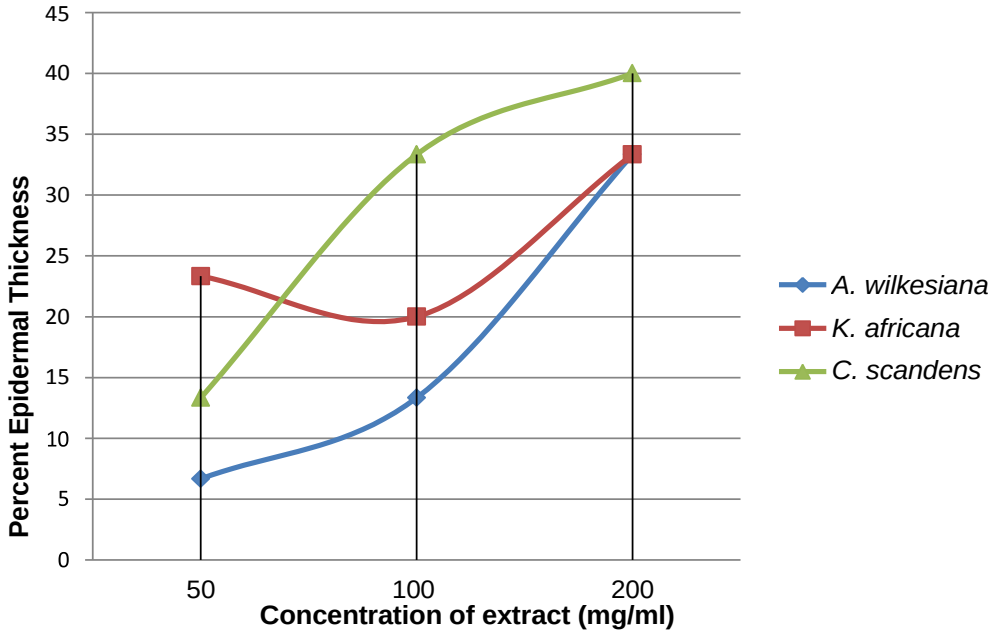

Figure 2. Change in percent epidermal thickness with concentration of hexane extract.

Acalypha wilkesiana ointments

A. wilkesiana ointments exhibited dose-dependent drug activity (Figures 1 and 2). The methanol ointments generally exhibited higher drug activity than the hexane extracts. Any particular progression was not observed for the irritation potential of the *A. wilkesiana* methanol extract ointment. For the hexane extract ointment, the irritation potential increased gradually with increasing extract concentration. No erythema was observed on the treated tail skin or elsewhere.

Culcasia scandens ointments

C. scandens had the least relative drug activity for both

the methanol and hexane extract ointments. A steady rise in the irritation potential of both the methanol and hexane ointments was observed (Figures 1 and 2). The *C.a scandens* methanol ointments had a lower irritation potential compared to the hexane ointments.

Comparison of the drug activity of *Acalypha wilkesiana*, *Caulcasia scandens* and *Kigelia africana*

Only the *A. wilkesiana* methanol extract ointment (200 mg/ml) showed greater than 40% drug activity which could be compared to the activity of *K. africana* ointments, thus, suggesting that it can be used in antipsoriatic drug development. The irritation potential of the *A. wilkesiana* hexane ointments was close to that of the *K. africana* stem hexane ointments, suggesting that it would be better to use the methanol extract that had a lower irritation potential with comparable drug activity The *C. scandens* ointments all had lower than 40% drug activity.

Conclusion

Using the modified mouse tail model, the *A. wilkesiana* showed more prospects of being an anti-psoriatic topical agent when compared to *C. scandens* and *K. africana* as its drug activity was quite similar to that of *K. africana*, while its methanol extract had a lower irritation potential and did not cause erythema. However, more pre-clinical tests need to be carried out on the three plants using other models to ascertain their anti-psoriatic activity and how they respond to other aspects of psoriasis, considering the complex nature of the disease.

CONFLICT OF INTERESTS

The authors have not declared any conflict of interests.

REFERENCES

Adesina SK, Idowu O, Ogundaini AO, Oladimeji H, Olugbade TA, Onawunmi GO, Pais M (2000). Antimicrobial constituents of the leaves of Acalypha wilkesiana and Acalypha hispidia. Phytotheraphy Res. 14(5):371-374.

Agrawal U, Mehra NK, Gupta U, Jain NK (2013). Hyper branched dendritic nano-carriers for topical delivery of dithranol. Informa healthcare. J. Drug Target. 21(5):497-506.

Alade PI, Irobi ON (1993). Antimicrobial activities of crude leaf extracts of Acalypha wilkesiana. J. Ethnopharm. 39(3):171-174.

Bosman B, Matthiesen T, Hess V, Friderichs E (1992). A quantitative method for measuring antipsoriatic activity of drugs by the mouse tail test. Skin Pharmacol. Physiol. 5(1):41-48.

Dwarampudi LP, Dhanabal SP, Shanmugam R, Mumganthan N (2012). Antipsoriatic activity and cytotoxicity of ethanolic extract of Psoralla corylifolia seeds. Hygeia: J. Drugs Med 4(2).

Elujoba AA, Odeleye OM, Ogunyemi CM (2005). Traditional medicinal development for medical and dental health care delivery system in Africa. Afr. J. Trad. Complement. Altern. Med. 2(1):46-61.

Fawehinmi AB, Lawal H, Etatatuvie SO, Oyedeji FO (2013). Preliminary phytochemical screening and antimicrobial evaluation of four medicinal plants traditionally used in Nigeria for skin infection. Afr. J. Pure. Appl. Chem. 7(2):44-49.

Haruna MT, Anokwuru CP, Akeredolu AB, Akinsemolu A, Alabi OA (2013). Antibacterial and antifungal activity of Acalypha wilkesiana. Eur. J. Med. Plants 3(1):52.

Kofi-Tsekpo M (2004). Institutionalization of African traditional medicine in health care systems in Africa. Afr, J. Health Sci. 11(1-2):i–ii.

Ledon N, Casaco A, Romirez, Gonzalez A, Cruz J, Gonzalez R, Capole A, Tolon Z, Rojas E, Rodriguez VJ, Merino N, Rodriguez S, Ancheta O, Cano MC (2007). Effects of a mixture of fatty acids from sugarcane (Saccharum officinorum L) wax oil in two models of inflammation: Zymosan – induced arthritis and mice tail test of psoriasis. Phytomedicine 14:690-695.

Mills E, Cooper C, Seely D, Kanfer I (2005). African herbal medicines in the treatment of HIV: Hypoxis and Surtherlandia: An overview of evidence on pharmacology. Nutr. J. 4:19.

Okoli CO, Akah PA (2000). A pilot evaluation of the anti-inflammatory activity of Caulcasia scandens a traditional antirheumatic agent. J. Altern. Complement. Med. 6(5):423-237.

Olatunji AG, Atolani O (2009). Comprehensive and scientific demulsification of Kigelia Africana: A review. J. Pure Appl. Chem. 3(9):158-164.

Oyedeji FO, Bankole-Ojo OS (2012). Quantitative evaluation of the antipsoriatic activity of sausage tree (Kigelia Africana). Afr. J. Pure. Appl. Chem. 6(13):214-218.

Oyeneye OY, Orubuloye IO (1985). Some aspects of traditional medicine in Bendel State of Nigeria: An exploratory study. NISER monograph series, No 14. NISER.

Papp K, Cather JC, Rosop L, Sofen H, Langley RG, Matheson RT, Hu C, Day RM (2012). Efficacy of a ptrmilast in the treatment of moderate to severe psoriasis: a randomized controlled trial. The Lancet 380(9843):738-746

Sangita S, Kaur H, Ripudaman BV, Singh SK (2009). Kigelia Africana (Lan) Benth - An overview. Nat. Radiance 8(2):190-197.

Sambo LG (2010). The decade of African traditional medicine: Progress so far. African traditional medicine day. 31 August. The African Health Monitor pp4 WHO – AFRO.

Schaper K, Dickaut J, Japtok L, Kietchmann M, Mischke R, Kleuser B, Baumer W (2013). Spingosine – 1- Phosphate exhibits anti-proliferative and anti- inflammatory effects in mouse models of psoriasis. J. Dermatol. Sci. 71(1):29-36.

Sebok B, Bonnekoh B, Kerenyi M, Gollnick H (2000). Tazarotene induces epidermal cell differentiation in the mouse tail test used as an animal model for psoriasis. Skin Pharmacol. Appl. Skin Physiol. 13(5):285-291.

Singhal M, Kansara N (2012). *Casssia tora* L. creams inhibit psoriasis in mouse tail model. Pharmaceut. Crops 3:1-6.

Suresh PK, Singh P, Saraf S (2013). Novel topical drug carriers as tool for psoriasis. Progress and advances. Afr. J. Pharm. Pharmacol. 7(5):138-147.

Wong JW, Koo JYM (2012). The safety of systemic treatments that can be used for geriatric psoriasis patients: A review. Dermatol. Res. Pract. Article 3674654.