The use of totarol to treat acne in an adolescent:

A case study

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Introduction

This case reports the use of totarol in the form of an alcohol-based topical medication followed by a totarol-containing moisturiser, for the treatment of acne vulgaris in an adolescent. The practice was made aware of the existence of these products and was offered the opportunity to try them. It is anticipated that these products will be commercially available nationwide by the time of publication.

Case history

The patient was a 14-year-old Caucasian male with a 14-month history of acne vulgaris. He had previously tried Clearasil Medicated Wipes, with little success. These contain 2% salicylic acid – a keratolytic agent – and ethanol. The patient initially presented for an unrelated medical problem and was offered the opportunity to try the totarol products to treat his acne. He consented to trying the products and to having his photograph taken from time to time to monitor the products' effects.

The treatment regime consisted of applying the alcohol-based topical medication, followed by the totarol-containing moisturiser, twice daily. He applied the products to the areas of his face that had particularly prominent acne. He continued this twice daily for four weeks, then once daily for two weeks (patient's discretion to change the frequency of application). His photograph was taken at intervals throughout the treatment period.

Background to totarol

Totarol is a natural extract from heartwood of the Totara tree (*Podocarpus totara*).[2] It is also extractible from other podocarps including rimu, some trees in the cypress family (cypress, juniper, thuja); and rosemary.[2] It is most abundant in Totara trees.[2] The extraction process[2] is called 'supercritical extraction'. This is a process that uses high pressure carbon dioxide under defined conditions of temperature, pressure and gas flow to extract totarol from powdered Totara deadwood (in the form of old fence posts, telegraph poles, house piles, and so on). The process ensures that the extract and residual wood has no harmful solvent residues, and that the highest possible quality of extract is obtained. The water in the extracted product is then removed by freeze-drying. This extraction process results in a product containing approximately 60% totarol by mass.

Totarol is a broad-spectrum antibacterial, being active against *Staphylococcus aureus*;[3] methicillin-resistant *Staphylococcus aureus*[4] (epidemic, community, and multi-drug-resistant strains[2]); *Streptococcus mutans*;[3,5] penicillin-resistant *Streptococcus pneumoniae*;[6] Erythromycin-resistant *Streptococcus pyogenes*;[2] high-level-gentamicin-resistant Enterococcus faecalis;[6] vancomycin-resistant *Enterococcus faecalis*;[2] *Salmonella menston*,[5] *Eschericia coli*;[5] *Enterobacter aerogenes*;[5] *Pseu-*

Figure 1. Chemical structure: Totara-8,11,13-trien-13-ol; C20H30O[1]

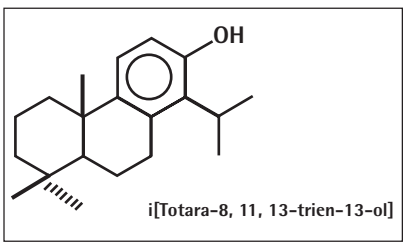
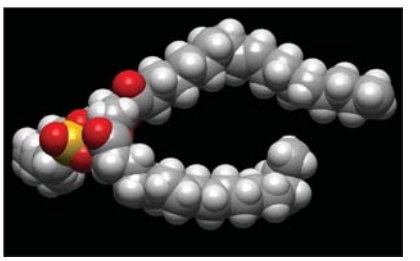


Figure 2. 3D totarol molecule



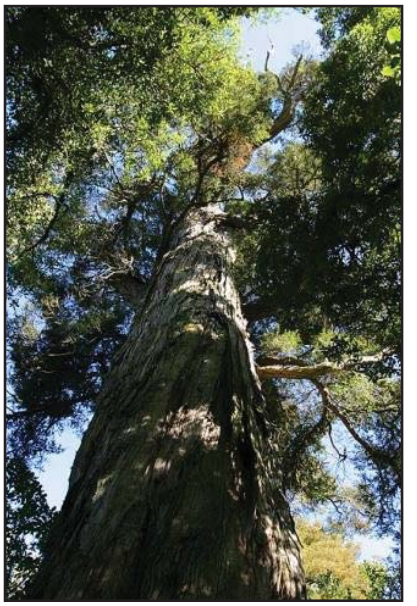
domonas aeruginosa;[5] *Bacillus subtilis*;[5] *Brevibacterium ammoniagenes*;[5] and *Propionibacterium acnes*.[3] Beta-amino alcohol derivatives of totarol have demonstrated antiplasmodial properties that have no cross-resistance with chloroquine.[7] Totarol from the Alaska Cypress tree (Yellow Cypress, Nootka Cypress, *Callitropsis nootkatensis*, *Chamaecyparis nootkatensis*[8]) has demonstrated activity against *Mycobacterium tuberculosis*.[9]

Totarol's mechanism of antibacterial activity is not known, however some authors have suggested that it compromises the functional integrity of cell membranes.[10] Haraguchi et al. studied totarol's actions on Pseudomonas and discovered that it inhibited oxygen consumption and respiratory-driven proton translocation in whole cells, and oxidation of NADH in membrane preparation (by inhibiting a number of NADH-related enzymes).[11] Evans et al. alternatively suggested that it disrupts bacterial energy metabolism, although they admitted that this action occurs at much higher concentrations than are significant for antibacterial activity.[6] Although the exact mechanism of action is not known, all proposed mechanisms are dissimilar to those of macrolides and tetracyclines. Thus cross-resistance of macrolide- and tetracycline-resistant bacteria to totarol seems unlikely. Unfortunately researchers have yet to produce a totarol-derived systemic antibiotic, since the potential benefits would seem to be considerable.

Totarol has been tested for safety in human applications. A skin irritation/sensitisation test of 0.05% totarol solution on 50 human subjects resulted in no evidence of any toxic effects on the skin.[12] Furthermore, totarol is not cytotoxic at concentrations required for antibacterial and antioxidant activity in cosmetic applications.[2] However, above these concentrations it can be.

Totarol therefore has potential for use in current practice as a topical agent for treatment of acne vulgaris.

Figure 3. Totara tree



Since totarol has antibacterial activity against a bacterium that is related to the development of acne, *Priopionibacterium acnes*, its potential use for aiding patients with acne is obvious. However a Pubmed search revealed no papers on totarol's application to clinical practice of any sort.

Totarol has already been marketed in an alcohol-based preparation for the treatment of acne, and in a moisturiser. However these products are not available on the market at the time of writing.

Results

Noticeable improvement in the patient's acne was seen over the period that he used the products.

There is an apparent reduction in inflammation and size and extent of lesions over the six week period. The patient was very pleased with the results achieved to date.

Discussion

Webster[13] summarises the pathophysiology of acne well:

'Acne vulgaris is caused by abnormal desquamation of the keratinocytes that line the sebaceous follicle, which creates a microplug or microcomedo. An increase in circulating androgens at the onset of puberty stimulates the production of sebum into the pilosebaceous unit. These events combine to create an environment within the pilosebaceous unit that is favorable for the colonization of the commensal bacteria, Propionibacterium acnes. With proliferation, P. acnes secretes various inflammatory molecules and chemotactic factors that initiate and perpetu-

Figure 4a. Totarol extraction

Figure 4b. Totarol extraction

Figure 5. Totarol powder

Figure 6a. Before treatment

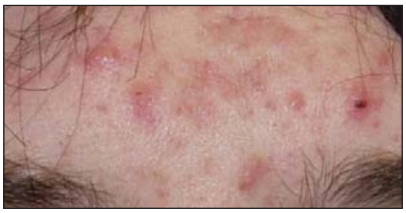
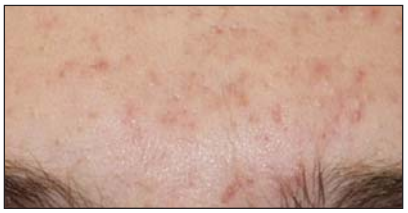


Figure 6b. Day 42 of treatment



ate the local inflammatory response and possibly induce keratinocyte hyperproliferation as well.'

Eradication of *P. acnes*, whether through systemic or topical antibacterial agents, improves the acne. Totarol falls into the class of topical antibacterial agents, with good activity against *P. acnes*, *S. aureus* of many types, and many other non-commensal bacteria. This patient tried topical totarol in an alcohol solvent and a moisturiser, without the concomitant use of keratolytics like salicylic acid or adapalene. The improvement as indicated in the photographs is obvious; a number of questions remain however. Is the change really due to totarol? Would the patient's acne have improved more or less if he had used a keratolytic as well? Would the patient's acne have improved more or less if he had used a systemic antibiotic as well?

This case provides anecdotal evidence of improvement in acne with the use of topical totarol; however to establish a causal relationship, large controlled trials are required. With use of a keratolytic concomitantly, there is the theoretical advantage of improved pilosebaceous drainage, and perhaps better antibiotic penetration into the colony. However some experiments have demonstrated inhibition of antibacterial activity when certain antibacterials (not totarol) have been used in combination with other agents. Others have given evidence of reduction in bacterial resistance and acne with in vitro and in vivo use of ancillary agents such as zinc salts.[14] Therefore trials of totarol in combination with other agents are required.

With the possibility of future long-term and widespread use of totarol for acne, one might also wonder whether bacteria would become resistant to totarol. Furthermore, would bacteria that are already resistant to erythromycin and/or tetracyclines be resistant to totarol already, or would they be sensitive? Current theory suggests that antibiotic-resistant organisms should be sensitive to totarol, but one cannot know for sure until more studies have been done. Studies on the long-term use of totarol alone for acne, against already antibacterial resistant organisms, and in conjunction with other antibacterials, would also be valuable.

Conclusion

This case report documents improvement in acne following regular application of an alcohol-based totarol product and a totarol-containing moisturiser. Totarol has good theoretical reasons for it to be a useful agent in the treatment of acne, and has tested as safe for topical (non-pregnant/non-lactating) human use. This is the first case report that we could find of medicinal use of totarol, so at this early stage rigorous data is absent. More research is therefore required in the form of larger clinical trials.

Acknowledgements

Paul Williams, Mende Biotech Ltd

Competing Interests

Dr Nixon is medical advisor to Mende Biotech Ltd. At the time of writing this is an unpaid position.

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