

Clinical efficacy and Safety of *Mimosa tenuiflora* Bark Extract in the Rhagades of the Nipple

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SUMMARY: Clinical efficacy and Safety of *Mimosa tenuiflora* Bark Extract in the Rhagades of the Nipple.

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Rhagades of the nipple are an inflammatory disease that, during puerperium, could condition breast-feeding. No specific drug treatments are available so far. A topical preparation mainly based on the extracts of Mimosa tenuiflora bark, having healing and skin regenerating activity, and of Calendula officinalis for its synergistic action. A clinical study was carried out to evaluate the efficacy and safety of this cream formulation in the treatment of breast rhagades in 65 lactating women, mean age 30.6 years, with rhagades of the nipple. The cream was applied at each suckling, 6.3 times a day on average, for 4 weeks. Bleeding rhagades healed in 95.6% of cases within 48-72 hours. Fissures and erythema relieved until their total disappearance and nipple elasticity improved in 81.5% of cases. There was no need to withdraw lactation, except for 3 cases that did not show benefits. Physician's and mothers' final judgement on drug efficacy was very good in more than 95% of cases and all the babies manifested their good acceptance. No adverse reactions were complained by the mothers and babies.

KEY WORDS: rhagades of the nipple, *Mimosa tenuiflora*, bark extracts.

Introduction

Rhagades of the nipple are the expression of an inflammatory disease occurring during puerperium that could condition breast-feeding. Etiopathogenesis of rhagades of the nipple is still not well defined, but anyway the risk to evolve to an infection is high. Moreover, the resolution of rhagades is a priority in order to avoid the possibility that the mother discontinues breast-feeding due to this very painful disturbance. For these reasons, the first objective of rhagades treatment is to heal rapidly the lesion, to block the access of germs and to reduce pain, minimising the risks of complications and breast-feeding discontinuation.

No specific drug therapy is available so far: the present symptomatic and often empirical treatments adopted are mainly aimed to relieve pain. Bibliographic references are scarce and backdated: estrogens (1), steroids (2-4), antimycotics (5), antibiotics (4), chlorophyll (6) never entered the daily practice.

Important issues in the choice of the treatment

are the concern of the mother to use any products that could interfere with the safety of the child, and the risk to overtreat inappropriately a non-infected lesion.

It is not less important that breast-feeding be continuous and long-lasting, even beyond the 2nd year: the lack of compliance could condition the production of milk, and hence, the same maintenance of maternal breast-feeding (7).

According to these premises, the use of active natural products should be preferred for their potential safety.

A topical preparation based on extracts of *Mimosa tenuiflora* bark, having healing and skin regenerating activity, and of *Calendula officinalis* for its synergistic action was developed. The bark extract of *Mimosa tenuiflora* is a remedy employed in the traditional medicine coming from Maya civilisation to cure wounds, burns and ulcers.

The catastrophic events which occurred in Mexico during the 1980 decade, (the eruption of the volcano Chichonal in Chiapas in 1982, the dramatic natural gas explosion in San Juan Ixhuatepec in 1984, the earthquake in 1985, the airliner crash in Toluca in 1986) responsible for a remarkable number of skin wounds and burns and the resulting high request for appropriate therapies, prompted to find sources

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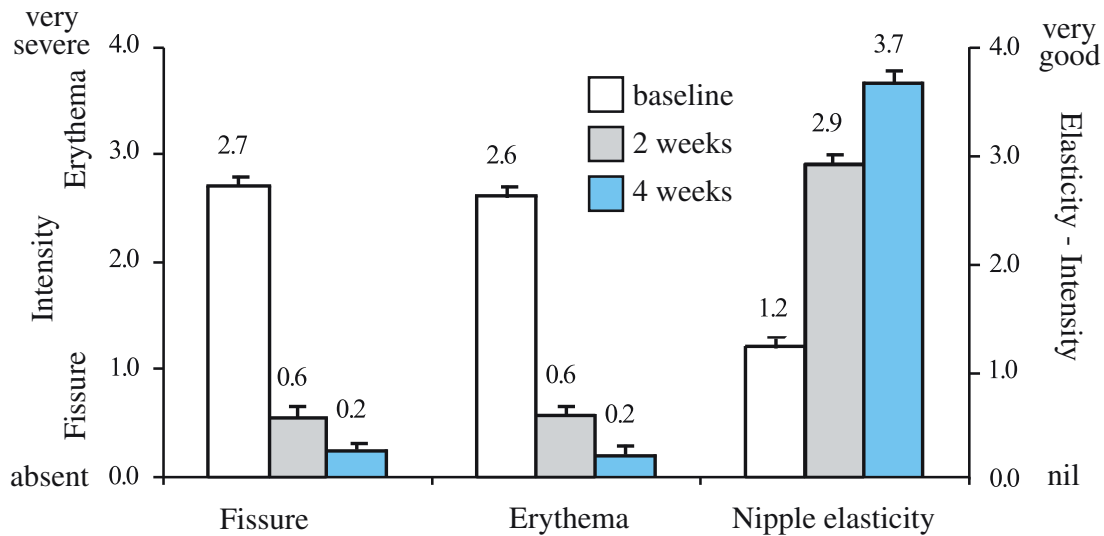


Fig. 1 - Fissures, Erythema, Nipple elasticity during the treatment with Anti-rhagades Cream (mean ± SEM).

for the relevant treatment (8). This requirement led to use officially an agent adopted at that time by popular medicine: namely the bark of tepescohuite, taxonomically corresponding to *Mimosa tenuiflora* (Willdenow) Poiret, which now has become known as “tree of the skin” for its action of facilitating skin regeneration and scar prevention (9-12). The people of Chiapas (Mexico) obtained from the *Mimosa tenuiflora* bark a brown powder that was directly sprinkled on the injured skin to form a firm crust: under this layer the damaged skin is protected from infections and the clean and fast process of wound healing was stimulated (13).

The bark contains saponins, lipids, phytosterols,

methoxychalcones, kukulkanins, and mainly tannins, which exert an antibacterial, antimycotic, astringent action as well as an action against free radicals (8, 12-16).

The extract of *Calendula officinalis* has a synergic action with *M. tenuiflora* extract thanks to its content in triterpendiol esters, which possess anti-inflammatory, anti-edematous, antibacterial, antioxidant activities, and, very relevant to the present indication, stimulate the regeneration of new epithelium in skin lesions (17-20, 21). The formulation is completed by the presence of vitamin A that plays a role in cell regulation and differentiation, particularly at the epithelial level. An adequate concentration of vitamin

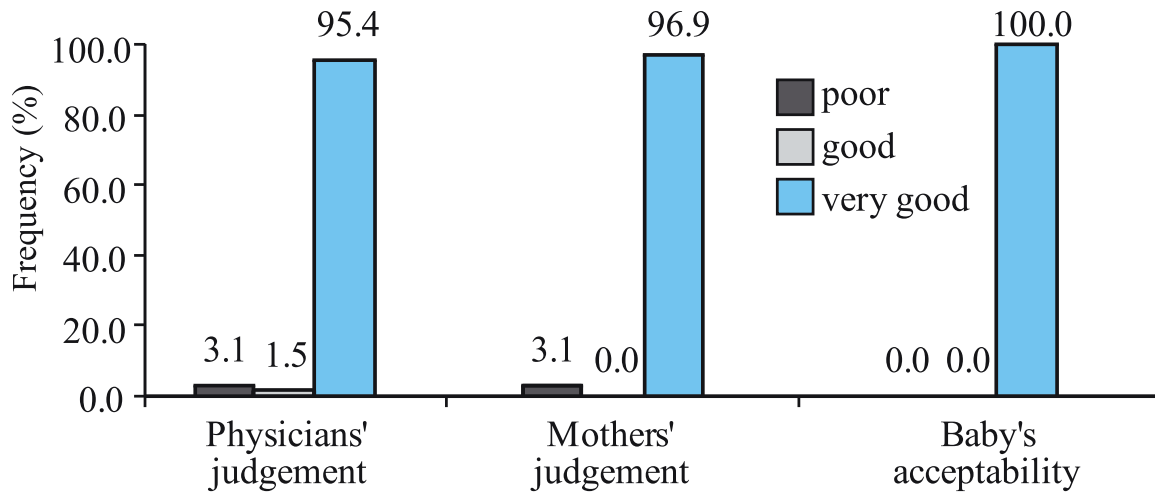


Fig. 2 - Physicians', mothers' and babies' final judgement on efficacy and acceptability of the Anti-rhagades Cream.

A controls the functional and structural integrity of epithelial cells, as it stimulates the epithelial basal cells to produce mucus whose suppression causes irritations and infections. On the other hand, vitamin E is characterised by a marked antioxidant effect. Both vitamins can reduce the damage caused by free radicals and play an important role in maintaining the physiologic trophism of the skin (22).

Besides the empirical and anecdotic reports of activity of the individual components, no clinical data are available so far on this combination in this specific pathology. The purpose of the study was to evaluate the efficacy and safety of this new topical formulation based on the bark extract of *Mimosa tenuiflora* in the treatment of rhagades of the nipple occurring during breast-feeding.

Patients and methods

The selection criteria for this open-label study considered breast-feeding women in which rhagades of the nipple occurred. Patient's history and clinical conditions were registered at baseline, then the women were treated with the cream applied after each suckling for 4 weeks, without the need of washing the skin after the application. The topical preparation contained the bark extract of *Mimosa tenuiflora*, the extract of *Calendula officinalis*, vitamin A and E (Saugella Crema Antiragadi Seno). No other cream was used during the study. Once a day, the nipple was washed with an appropriate detergent.

The clinical evaluation was carried out at baseline, and after 2 and 4 weeks of treatment. Fissure and erythema were scored with the following scale 0 =

absent, 1 = mild, 2 = moderate, 3 = severe, 4 = very severe, while nipple elasticity was evaluated according to the score 0 = null, 1 = poor, 2 = moderate, 3 = good, 4 = very good. A final overall judgement was expressed by the physician (efficacy), by the mother (tolerability) and the baby (acceptability) at the end of the treatment with the score 0 = null, 1 = poor, 2 = moderate, 3 = good, 4 = very good.

The case report form contained a specific section to record the adverse reactions of the mother or of the baby.

Results

Sixty-five lactating mothers, mean age 30.6 years \pm 4.8 (SD, range 20-43), presented with rhagades of the nipple. The characteristics of the population studied were: Caucasian race 95.2%, primiparous women 46.2%, term delivery 92.2%, vaginal delivery 53.1%. Breast-feeding started at the 2nd day in 40.7% of cases, and at the 3rd day in 42.4% of cases.

The cream was applied after each suckling, 6.3 times a day on average, 6 times a day for the 53.6% of the mothers and 7 times for the 35.7% of mothers.

Bleeding rhagades healed in 95.6% of cases within 48-72 hours. Fissures and erythema relieved up to their total disappearance in 89.2% and in 93.8% of cases, respectively, and nipple elasticity improved in 81.5% of cases (Fig. 1). There was no need to discontinue breast-feeding, save 3 cases that did not improve.

Physician's and mothers' final judgement of the efficacy was very good in more than 95% of cases and all the babies declared their good acceptance (Fig. 2).

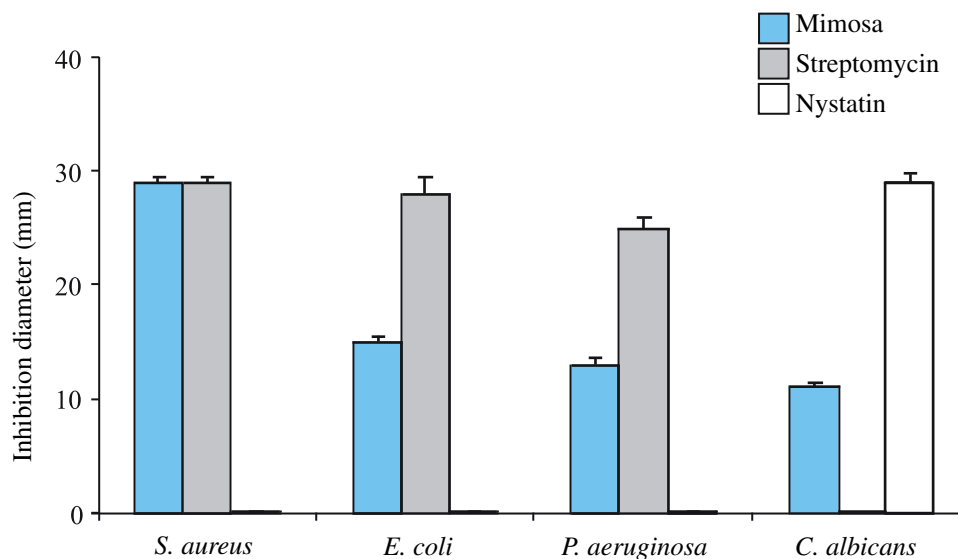


Fig. 3 - Antimicrobial effect of *Mimosa tenuiflora* bark extract with the agar diffusion method (5 mg/0.1 mL of aqueous extract).

The investigators rated as poor only 2 cases, in agreement with the mothers' evaluations. No adverse reactions were complained by the mothers and babies.

Discussion

The clinical data of the present study showed the remarkable efficacy of the topical treatment based on the use of the bark extract of *M. tenuiflora* in healing rhagades of the nipple in lactating women. Tolerability of the formulation was excellent, which confirms the experimental data on safety. In fact, as toxicity is concerned, *M. tenuiflora* bark extract was judged to be non-irritant in the animals after single and repeated applications on the skin (23-24). Moreover, it is devoid of mutagenic action (25).

The potential of *M. tenuiflora* bark extract of inducing a delayed contact hypersensitivity was evaluated in skin sensitisation tests in Guinea-pigs: neither clinical signs nor cutaneous reactions were detected versus controls, though the same animals were just used in a previous study showing a sensitisation response to a positive sensitiser (40).

In conclusion, this anti-rhagades cream favours the formation of a new cutaneous structure, due to the antibacterial and antimycotic activity which allows to concomitantly counteract both *Candida albicans*, often put in relationship with the onset of rhagades, and overlapping bacterial infections. The microbiological activity profile of *Mimosa tenuiflora* bark extract showed its antibacterial and antimycotic

properties with a clear growth inhibition of gram positive (*Staphylococcus aureus*), gram negative (*Escherichia coli* and *Pseudomonas aeruginosa*) and fungi (*Candida albicans*). Its inhibiting action is lower than streptomycin on gram negative and than nystatin on *Candida*, but anyhow it covers a wider range versus the antibiotic and the antimycotic drugs taken alone (13) (Fig. 3). The healing and protective effect of the skin against breast rhagades is the result of the pharmacological properties of all the components of the end formulation and it is also possible due to the compatibility of *M. tenuiflora* bark with animal tissues. This characteristic was shown by transplanting a callous graft of *M. tenuiflora* into the subcutaneous tissue of rats: the vegetable cells survived in the animal environment, suggesting the possibility of an *inter-regni* transplantation (27).

M. tenuiflora extract was found to be active on cell reproduction when applied topically to Guinea-pig teat *in-vivo*, with the colchicine test, a substance which inhibits mitoses (28). In fact, an increase in the mitotic index of mammary cells was observed after application of *M. tenuiflora* extract for two weeks versus controls. The astringent effect and the increased capillary resistance enhances the skin impermeability, which is further protected by the antioxidant action of vitamins A and E. The fast healing and pain relieving actions of the anti-rhagades cream reduce the risks of discontinuation of maternal lactation. Its preventive use should be clinically tested in late pregnancy in women predisposed to rhagades.

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