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WOUND HEALING PROFILE OF SEPTILIN

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Summary : Septilin, a proprietory preparation claimed to be useful in inflammatory conditions was tested for anti-inflammatory and wound healing effects in albino rats. It significantly enhanced gain in tensile strength in incision wounds and wound contraction and epithelization in excision wounds. It also suppressed acute inflammation (rat paw edema) significantly without affecting chronic inflammation (cotton pellet granuloma).

Key words : Septilin tensile strength epithelization wound contraction rate paw edema cotton pellet granuloma

INTRODUCTION

Septilin* is a proprietary herbal preparation said to be helpful in gram positive and gram negative infections (1, 2). Balsamodendron mukul (Guggul) and Rubia cordifolia present in Septilin are alleged to have anti-inflammatory and wound healing promoting actions (3, 4). Conversely, anti-inflammatory drugs like aspirin and other NSAIDs have been shown to suppress wound healing (5, 6). Hence, Septiling was tested for its wound healing and anti-inflammatory properties in rats.

Since there is no single wound model that helps monitoring the progress in various phases (e. g., granulation, collagenation, collagen maturation, epithelization and wound contraction) of healing, it becomes necessary to employ different wound models, each providing information on changes in specific phases of healing. In this study three different models of wounds have been employed.

* Composition : (i) Balsamodendron mukul (Guggul), (ii) Maharasnadi quath, (iii) Exts. Phyllanthus emblica, (iv) Exts. Tinospora cordifolia, (v) Exts. Rubia cordifolia, (vi) Moringa pterygosperma, (vii) Pristimera indica, (viii) Shankh Bhasma.

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MATERIALS AND METHODS

Albino rats of either sex weighing between 150-200 g were used. Wounds were made under sedative dose of pentobarbitone (2 mg/100 g, ip) supplemented with ether anaesthesia. Wounds were not dressed or covered and no chemotherapy was used. Animals used in each group (n=6—8) were weighed at the beginning and at the end of experiment.

The drug was given either orally as 20% aqueous suspension, (500 mg/kg) or applied locally (in case of excision wound only) as 8% ointment in soft paraffin once a day. Control animals received respective vehicle either orally or locally. The oral dose was computed for rats (7) from clinically recommended highest dose.

Excision wounds : Employing the method of Morton and Malon (8) excision wound was created by cutting away a circular piece (500 mm^2) of skin in its full thickness from inter-scapular region to monitor wound contraction and period of epithelisation. The wound contraction was calculated as percent reduction in wound area. The progressive changes in wound area were monitored, planimetric-

ally by periodically tracing the wound margin on a transparent paper with 1 mm^2 scale. The days required for falling off of eschar leaving no raw wound was taken as the period of epithelisation. Drug administration was continued till healing was complete (ranging from 12-22 days).

Dead Space wounds : The dead-space wounds were produced by subcutaneous implantation of pre-weighed and sterilised cotton pellet cut from dental rolls, one in each groin and axilla. Drugs were administered for 9 days. Weights of 10 day old granuloma (9) so harvested were noted after overnight drying at 60°C and expressed as mg % of the body weight (10).

Incision wounds : Two 6 cms long paravertebral skin incisions were made on either side according to the method of Lee (6). After mopping the wounds dry, the edges were approximated with interrupted silk thread sutures one centimeter apart. The sutures were removed on 7th post-operative day. Drug administration was continued upto 9th day. On 10th day the tensile strength was measured by the method of Lee (6).

Acute inflammation : By employing the method of Winter et. al. (11) carageenan-induced paw edema was measured at 0 and 3 hr and compared with that of control. Drug was given orally 30 min before carageenan challenge.

Chronic inflammation : The method employed was same as for dead space wound (vide supra).

Statistical analysis was done by student's 't' test.

RESULTS

Excision wound : As can be seen in fig. 1, Septilin showed significant ($P<0.001$) reduction in epithelisation period (in days) both on local (12.3 ± 0.3) and systemic (13 ± 0.5) administration compared to the control. Comparison of vehicle effect showed that topical vehicle enhanced epithelisation and reduced the epithelisation period from 21.9 ± 0.8 days (oral vehicle) to 17.7 ± 1.8 days. Wound contraction (Fig. 1) was significantly faster throughout in all animals reeeiving septilin orally or topically. Here again, the topical vehicle appears to favour contraction. Even though topical application of Septilin appeared to be more effective than oral Septilin, it may be apparent than real since soft paraffin used as topical vehicle had a pro-healing effect.

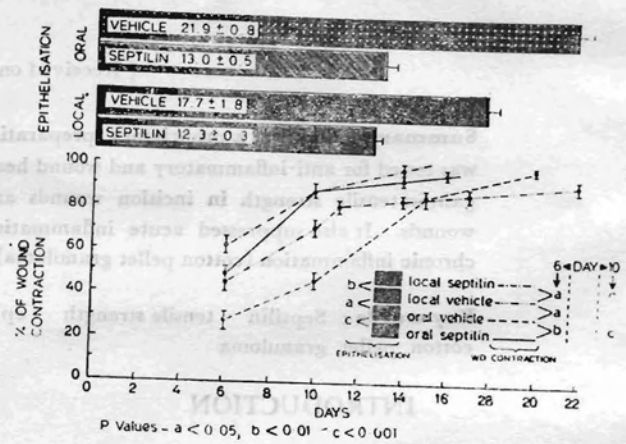

Fig. 1. : Effect of Septilin local and oral on epithelization (Bars) and wound contraction (lines) in excision wounds.

Dead space wound : The granuloma weight in animals receiving Septilin was not significantly (165.5 ± 13.1 mg % of body weight) different from control value (157.2 ± 16.4 mg % of body weight).

Incision wound : Septilin significantly ($P<0.001$) raised the tensile strength from control value of 281.9 ± 13.7 to 408.8 ± 17.4 g. (Fig. 2A)

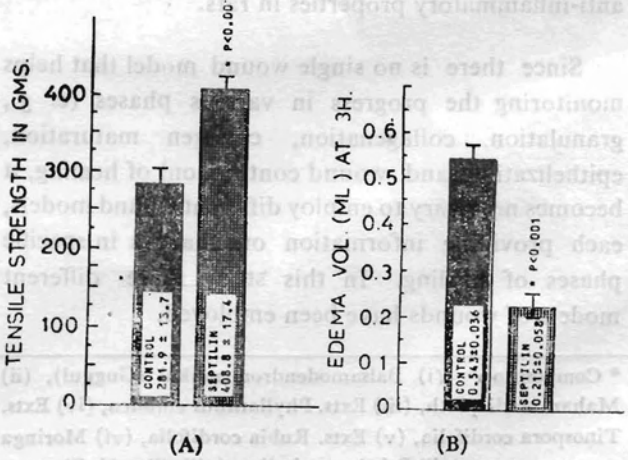

Fig. 2. : Effect of Septlin on :(A) tensile strength of 10 days old incision wounds (left panel) and (B) rat-paw edema 3 hr past carrageenan injection (right Panel).

Acute inflammation : Septilin exhibited anti-inflammatory action as shown by significant ($P<0.001$) reduction in paw volume at 3 hr (Fig. 2B).

Chronic inflammation : Septilin failed to induce a significant change in dry weight of cotton pellet granuloma (ref. dead space wound results).

DISCUSSION

Inflammation is a forerunner of wound healing (12). Both steroidal (13) and non-steroidal anti-inflammatory agents (5, 6) are known to suppress healing. In view of this it was felt worthwhile to investigate the anti-inflammatory (3) and prohealing properties (4) of Septilin.

As indicated in the introduction, three different wound models were used to monitor influence of Septilin on different phases of healing. The results show that the drug promoted gain in tensile strength in incision wound models, but at the same time did not modify granulation phase of healing (dead space wound). Since granulation phase involves fibroblast proliferation and collagen laying, it may appear surprising that Septilin which fails to modify this phase of healing could still promote gain in tensile strength. Perhaps Septilin promotes cross-linking of collagen and its maturation. It is the cross linking and maturation of collagen and not its mass that determines the tensile strength (14). In case of excision wound Septilin promotes epithelisation and wound contraction whether the drug is given orally or applied topically. Though the present study can not answer as to the cause for such an action, it could be that the drug promotes migration and mitosis of epithilial cells and promotes contractions of myofibroblasts, the latter are now recognised as responsible for wound contraction (15).

Thus, the drug appears to promote some but not other phases of healing. This is not surprising. There are reports that drugs can differentially modify phases of healing (16; 17, 18, 19, 20). Such a differential action is possible since the various phases of healing progress concurrently and independent of each other (14).

As to the anti-inflammatory activity of Septilin, it was found to suppress carrageenan edema, but not granuloma weight. This differential action is conceivably possible since mediators like PGE, promoting the vascular phase of inflammation leading to edema, act differently on chronic (proliferative) phase and suppress it (21).

Use of nonsteroidal anti-inflammatory agents (NSAIA) is advocated (22, 23) to control post operative edema and pain. Since the NSAIAs have adverse effect on scar tensile strength as shown in animal studies (5, 6) it would be interesting to explore septilin clinically, as an alternative to NSAIAs. Proepithelisation property of Septilin may be of value in case of excision wounds and in burns.

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