Wound Healing Profile of Septilin

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ABSTRACT

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

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

*Composition:
Balsamodendron mukul (Guggul)
Exts. Maharasnadi quath
Phyllanthus emblica
Tinospora cordifolia
Rubia cordifolia
Moringa pterygosperma
Glycyrrhiza glabra
Shankh bhasma.

Since there is no single wound model that helps monitoring the progress in the various phases (e.g., granulation, collagenation, collagen maturation, epithelisation 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.

MATERIAL AND METHODS

Albino rats either sex weighing between 150-200 g were used. Wounds were made under sedative dose of pentobarbitone (2 mg/100 g, ip) supplemented with either 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 the 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 from the clinically recommended highest dose.

Excision wounds: Employing the method of Morton and Malon excision wound was created by cutting away a circular piece (500 mm²) of skin in its full thickness from the inter-scapular region to monitor the 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,
planimetrically by periodically tracing the wound margin on a transparent paper with 1mm² 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 granuloma⁹ so harvested were noted after overnight drying at 60°C and expressed as mg % of the body weight¹⁰.

*Incision wounds:* Two 6 cm 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 the 7th post-operative day. Drug administration was continued upto the 9th day. On the 10th day the tensile strength was measured by the method of Lee.⁶

*Acute inflammation:* By employing the method of Winter et al,¹¹ carrageenan-induced paw oedema was measured at 0 and 3 hours and compared with that of control. The drug was given orally 30 min before carrageenan challenge.

*Chronic inflammation:* The method employed was the 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 receiving 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.

*Dead-space wound:* The granuloma weight in animals receiving Septilin was not significantly (9165.5 ± 13.1 mg% of body weight) different from the control value (157.2 ± 16.4 mg% of body weight).
**Incision wound**: Septilin significantly (P<0.001) raised the tensile strength from the control value of 281.9 ± 13.7 to 408.8 ± 17.4. (Fig. 2A).

**Acute inflammation**: Septilin exhibited anti-inflammatory action as shown by significant (p<0.001) reduction in paw volume at 3 hours (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. Both steroidal and non-steroidal anti-inflammatory agents are known to suppress healing. In view of this it was felt worthwhile to investigate the anti-inflammatory and prohealing properties of Septilin.

As indicated in the introduction, three different wound models were used to monitor the 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 the 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 and maturation of collagen and not its mass that determines the tensile strength. In case of excision wound Septilin promotes epithelisation and wound contraction whether the drug is given orally or applied topically. Though the present study cannot provide an answer for the cause for such an action, it could be that the drug promotes migration and mitosis of epithelial cells and promotes contractions of myofibroblasts, the latter being now recognised as responsible for wound contraction.

Thus, Septilin 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. Such a differential action is possible since the various phases of healing progress concurrently and independent of each other.

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

The use of non-steroidal anti-inflammatory agents (NSAIAs) is advocated to control post-operative oedema and pain. Since the NSAIAs have adverse effects on scar tensile strength, as shown in animal studies, it would be interesting to explore Septilin clinically, as an alternative to NSAIAs. Pro-epithelisation property of Septilin may be of value in case of excision wounds and in burns.

**ACKNOWLEDGEMENT**

The authors are thankful to the college authorities for permission to conduct this study and to The Himalaya Drug Co., for free supply of Septilin tablets.
REFERENCES


