Wound Healing

The Effects of Topical Antimicrobial Agents

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The effect of four commonly used topical antimicrobial agents on the rate of reepithelialization of clean wounds was evaluated in white domestic pigs. Neosporin Ointment was found to significantly increase the rate of reepithelialization by 25%, while Furacin significantly retarded the healing rate by 24%. Pharmadine, a preparation containing povidone-iodine, did not affect the rate of healing. Both Silvadene and its vehicle significantly increased the rate of reepithelialization by 28% and 21%, respectively. The effects of these agents cannot be explained on the basis of their antimicrobial activity.

(Arch Dermatol 115:1311-1314, 1979)

Topical antimicrobial agents have been widely used by dermatologists, surgeons, and family practitioners to prevent bacter§ixPxP79Px:x7jPxPxP(8)x97P(3(8¬)P7(:8):PcmT1qxTi7PT§ixPxPTdmT1qxP9PTb7(3rmatol

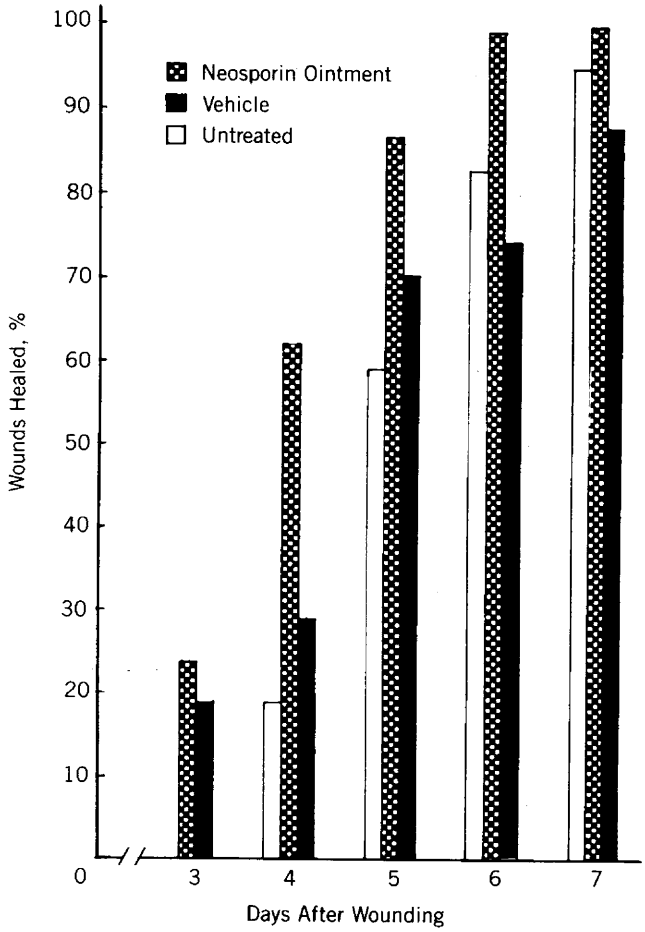

Fig 2.—Effect of Neosporin Ointment, vehicle, and control on wound healing.

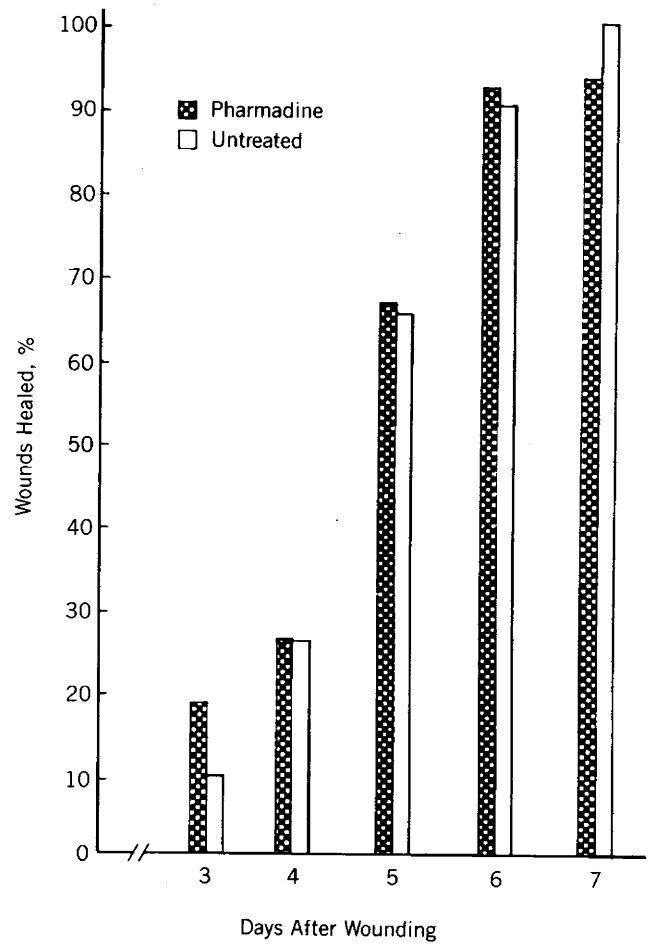

Fig 3.—Effect of Pharmadine and control on wound healing.

Table 1.—Effect of Agents and Vehicles on Healing*

Agent	Day 2	3	4	5	6	7
Neosporin group						
Untreated	0/17 (0)	0/27 (0)	5/27 (19)	19/32 (59)	25/30 (83)	20/21 (95)
Neosporin Ointment	0/19 (0)	5/21 (24)†	16/26 (62)‡§	26/30 (87)	26/26 (100)	19/19 (100)
Vehicle	0/15 (0)	5/27 (19)	8/28 (29)	21/30 (70)	20/27 (74)	22/25 (88)
Pharmadine group						
Untreated	...	2/20 (10)	5/19 (26)	17/26 (65)	18/20 (90)	13/13 (100)
Pharmadine	...	4/21 (19)	6/27 (27)	19/29 (66)	22/24 (92)	14/15 (93)
Furacin group						
Untreated	0/15 (0)	1/32 (3)	10/36 (28)	33/48 (69)	43/47 (91)	12/12 (100)
Furacin	0/14 (0)	0/21 (0)	1/27 (4)	2/34 (6)¶	17/32 (53)†	8/10 (80)
Vehicle	1/27 (4)	1/23 (4)	2/23 (9)	18/30 (60)	27/30 (90)	10/13 (77)
Silvadene group						
Untreated	0/59 (0)	4/71 (6)	35/86 (41)	44/77 (57)	...	...
Silvadene	0/15 (0)	14/29 (48)†	25/28 (89)¶	21/21 (100)	...	...
Vehicle	1/61 (2)	23/81 (28)†	78/93 (84)¶	83/90 (92)	...	...

*Values are expressed as number of specimens healed/total number of specimens tested. Numbers in parentheses are percent healed.
†$P < .05$ compared with untreated.
‡$P < .01$ compared with untreated.
§$P < .05$ compared with vehicle.
¶$P < .001$ compared with untreated.

Table 2.—Comparative Rates of Healing With Agents and Vehicles Tested

Agent	HT_{50}, Days*	Relative Rate of Healing Compared With Control, %
Neosporin group		
Untreated	4.8	0
Neosporin Ointment	3.6	+25
Vehicle	4.6	+5
Pharmadine group		
Untreated	4.6	0
Pharmadine	4.55	+1
Furacin group		
Untreated	4.6	0
Furacin	6.0	−24
Vehicle	4.8	−9
Silvadene group		
Untreated	4.3	0
Silvadene	3.1	+25
Vehicle	3.4	+21

*HT_{50} is the time needed for 50% of the wounds to heal.

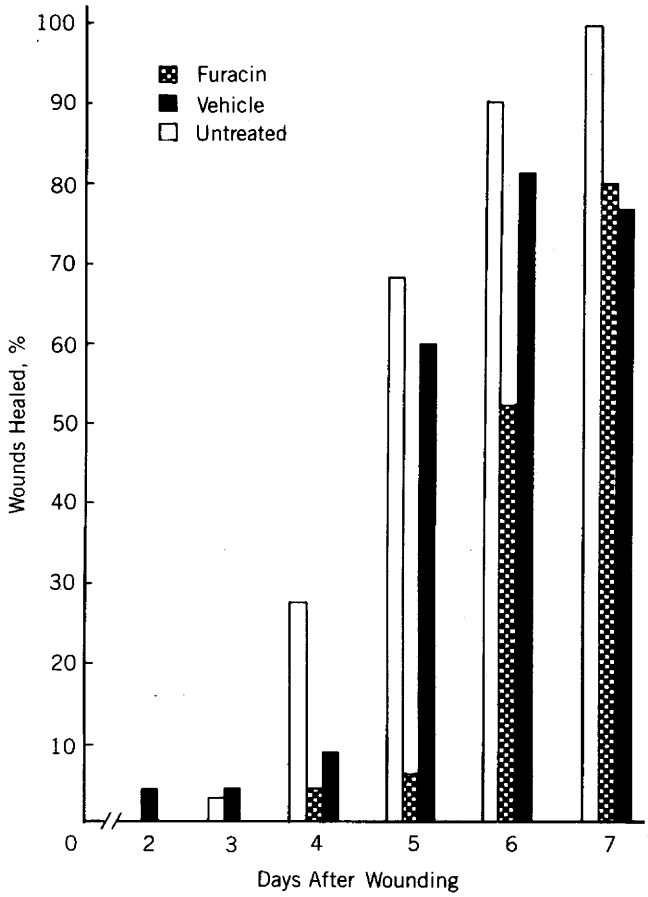

Fig 4.—Effect of Furacin, vehicle, and control on wound healing.

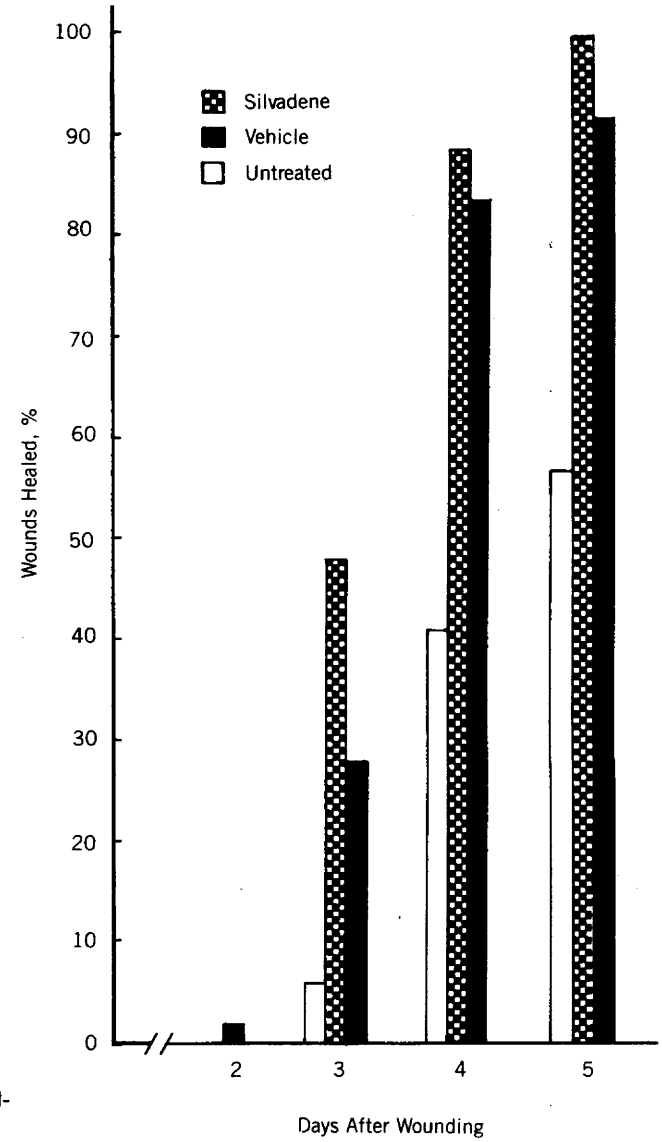

Fig 5.—Effect of Silvadene, vehicle, and control on wound healing.

crusts adhere to the dermal portion of the specimen and leave a defect unless epidermis is present beneath the crust

from curves generated by probit analysis of the data presented in Table 1.

topical agents can cause tissue toxicity, which might lead to a delay in

Treatment

Table 2.

The wounds on each experimental ani-

COMMENT

The rate of reepithelialization of a wound can be altered by changes in

three antibiotics, neomycin sulfate, polymyxin B sulfate, and bacitracin zinc, in a petrolatum base. This agent covers a wide spectrum of antibacterial activity including most Gram-positive and Gram-negative bacteria found in human and pig skin. We found that the active agent promoted healing by 25% compared with the untreated control. This increase was significant compared with both the vehicle and the control. However, there was no significant difference noted between the vehicle and the control.

Petrolatum products differ widely in their preparation and physical properties.2" The petrolatum vehicle of Neosporin Ointment has a lower melting point than United States Pharmacopeia petrolatum and differences in healing rates have been noted between the two. The petrolatum vehicle showed an insignificant increase in healing time compared with a significant slowdown of 17% reported previously with USP petrolatum.19 We confirmed the difference in the effect of these two types of petrolatum on healing in studies directly comparing these two.

Pharmadine is a povidone-iodine solution with 9% to 12% available iodine. Its antimicrobial spectrum includes Gram-negative and Gram-positive bacteria. The povidone-iodine solutions have gained wide use as prophylactic treatment for minor procedures and in preoperative preparation. Despite the large overlap in antibacterial activity with Neosporin Ointment, we did not find an increased healing rate in Pharmadine-treated wounds as was found in those wounds treated with Neosporin Ointment.

Furacin contains nitrofurazone in Solubase, which is a water-soluble base of polyethelene glycols. This agent is used primarily as adjunct therapy in second-degree burns. As noted with Neosporin Ointment and Pharmadine, Furacin was the only topical antimicrobial agent we examined that demonstrated an inhibition of healing. The 24% slowdown was statistically significant compared with Solubase and its control.

Silvadene cream contains 1% sulfadiazine silver in a water-miscible cream. This product has been used extensively for the treatment of burns. Its antibacterial activity covers a wide sprectrum of Gram-positive and Gram-negative bacteria and also fungi. Silvadene promoted healing at the fastest rate of the agents in the study, being 28% faster than the control. Both the active agent and its base were significantly faster than the untreated control. There was no significant difference between the active agent and its vehicle.

Although we have demonstrated that topical antimicrobial agents can alter the rate of reepithelialization, their mechanisms of action are not clear, and probably differ from each other. From analysis of our data it appears that the effect on healing produced by these agents is not due to their antimicrobial action. The effect of Silvadene cream vehicle relative to the cream containing the active agent minimizes the possibility that this product influences wound healing by its antibacterial effect. Since Neosporin Ointment's vehicle had no real effect on healing and Pharmadine's vehicle consists mostly of distilled water, it would seem reasonable that the two products would influence wound healing similarly because of the similarity in the antibacterial spectrums of their active agents. However, this is not the case (Tables 1 and 2). Since povidone-iodine solutions have little tissue toxicity14 and proven antibacterial action, the possibility of wounds not healing rapidly with Pharmadine treatment because of tissue toxicity or insufficient antibacterial activity is remote.

Although Furacin has an antibacterial spectrum comparable to two agents that we have found to promote wound healing, it was found to significantly retard the rate of reepithelialization. The mechanism of its antimicrobial action differs from other agents in this study in that it inhibits enzymes that are necessary for carbohydrate