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WOUND HEALING IN RATS WITH THE ANTIBIOTIC FUCIDIN

BY

J. CALNAN AND H. J. H. FRY

From the Department of Experimental Surgery, Postgraduate Medical School, Ducane Road, London, W.12

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Fucidin, a new antibiotic which is stated to improve wound healing, was fed to rats subjected to incised wounds on the back. There was a significant difference (at the 1% level) in tensile strength of five- and seven-day wounds, but none between Fucidin-treated rats and their controls.

The observation by Taylor & Bloor (1962), that wounds of patients treated with the antibiotic Fucidin appear to heal more quickly than expected, is interesting, and worthy of further study. The present investigation was designed and carried out to test this hypothesis under conditions where infection can play no part. Fucidin (the sodium salt of fusidic acid) is an antibiotic prepared from *Fusideum coccineum* (Godtfredsen, Roholt & Tybring, 1962), which is orally effective against staphylococci.

METHODS

The tensile strength of healed five- and seven-day wounds was measured using a Sandblom-Petersen (1953) tensiometer in a consecutive series of 32 Wistar albino rats.

Half the rats were given a standard dose of Fucidin, 10 mg in 25 ml. water/day (about 90 mg/kg) in their drinking-water bottles. Since the antibiotic is bitter in solution, honey was used to sweeten the water given to the trial rats and their controls. Fluid intake was restricted to 25 ml. (the average intake of a rat) for all animals to ensure that each rat under trial took its full dose of antibiotic, and in practice all did so. The *p*H of the honey-water was 4.0; at this *p*H the antibiotic in solution was unaltered and fully potent (Barber & Waterworth, personal communication).

From previous experience it was known that the tensile strength of a wound increases with time (a 7-day-old wound is stronger than a 5-day-old wound) and varies according to the weight of the animal (the heavier, and older, the rat, the stronger the wound). For this latter observation (Calnan & Fry, 1962) the regression equation is $y=1.7434x-23.256$, where y = mean strength of three back wounds in grams force and x = weight of the rat in grams; the correlation coefficient is 0.7413, which is significant at the 1% level of confidence.

A random block design was used, the time element being incorporated in the treatments and the weight factor between different blocks. There were thus four treatments: Five-day wounds with oral Fucidin for five days; seven-day wounds with oral Fucidin for seven days; five-day wounds, no drug; and seven-day wounds, no drug. Hence rats 1 and 2 were Fucidin-treated, 3 and 4 being their respective "controls." Each block of four treatments was repeated eight times. Between these four groups, comparisons may be made to estimate the effect of time or of the antibiotic on wound healing with the same standard error.

The weights of individual rats in any one block were as far as possible similar, but weights of animals differed between blocks. The rats were kept in individual cages at room temperature and on a standard pellet diet, Dixon's no. 86 (50% wheat, 25% barley, 7% fish meal, 6% bone meal, 5% brewer's yeast, 1% cod-liver oil, 1% salt).

Under ether anaesthesia and aseptic conditions, three horizontal wounds through the skin and panniculus carnosus muscle, down to the fascial layer, 4 cm long and 1.5 cm apart (previously marked in ink through a metal template) were made on the back of each rat. Each wound was then closed by interrupted fine silk sutures, the sutured wound sprayed with Polybactrin powder, and a sterile dry dressing applied and held in place by two turns of "Elastoplast" bandage. Five or seven days later the dressings were discarded, sutures removed, and the tensile strength of each wound measured *in situ*. All wounds were made by one surgeon while all tensiometer readings were made by the other. Neither surgeon knew which rat was in the "treated" or "control" group until his work was finished. Only one wound became infected.

RESULTS

These are presented in Tables 1 to 3.

The mean weights of the rats in all four treatment groups were very similar (Table 1), and by an analysis of variance there was no significant difference between the weights of animals in the various treatment groups. Weight, therefore, can be excluded as a source of bias influencing the result of this experiment.

TABLE 1
TENSILE STRENGTH OF WOUNDS AND WEIGHT OF RATS

Treatment groups	No. of rats	Mean tensile strength (in *g* force), and standard error	Mean body weight (g), and standard deviation
5-day wounds with Fucidin	8	128·6±13·41	109·5±47·69
5-day wounds, no drug	8	111·9±13·41	114·5±47·69
7-day wounds with Fucidin	8	189·6±13·41	105·5±47·69
7-day wounds, no drug	8	197·1±13·41	113·0±47·69

TABLE 2
TENSILE STRENGTH OF WOUNDS: ANALYSIS OF VARIANCE
Showing a significant difference between treatments but none between groups (blocks) of rats

Source of variation	Sums of squares	Degrees of freedom	Mean square	Variance ratio	Significance
Treatments	45,752·5	3	15,250·83	10·598	At 1% level
Blocks	9,358·0	7	1,336·86	0·929	Nil
Residual (error)	30,219·5	21	1,439·02	—	—
Total	85,330·0	31	—	—	—

The tensile strength of the wounds, however, showed significant differences. The analysis of variance (Table 2) demonstrated that there was no significant difference between the results of individual blocks, but that there was a difference between treatments. There was a significant difference (Table 3) at the 1% level of confidence between the strength of five-day and seven-day wounds, but no statistically significant difference in the tensile strength of the wounds of rats treated with Fucidin and their controls.

TABLE 3
COMPARISON OF TENSILE STRENGTH OF WOUNDS

Treatments compared	N	"t"	*P*	Significance
Time: Controls 5 day/7 day	16	3·6125	>0·01	Highly significant
Fucidin treated 5 day/7 day	16	4·1003	>0·01	
Drug: Fucidin-treated/controls 5 days	16	0·8833	<0·3	Not significant
7 days	16	0·3955	>0·7<0·6	

DISCUSSION

The present investigation has been unable to show any difference in the tensile strength of wounds of those rats given oral Fucidin when compared with their controls, although the technique used was sensitive enough to show a significant difference in tensile strength of five-day and seven-day-old wounds.

Although it may not be justifiable to extrapolate these results to man, it seems unlikely that Fucidin of itself improves the rate of wound healing apart from controlling wound infection.

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