THE DYNAMICS OF THE INFLAMMATORY PHASE OF SKIN WOUND HEALING IN RATS

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1. Introduction

We present a mathematical model representing the inflammation phase of wound closure considering its importance in that process. The wound healing phases and some importants components are illustrated in the Figure 1 and Figure 2, respectively.

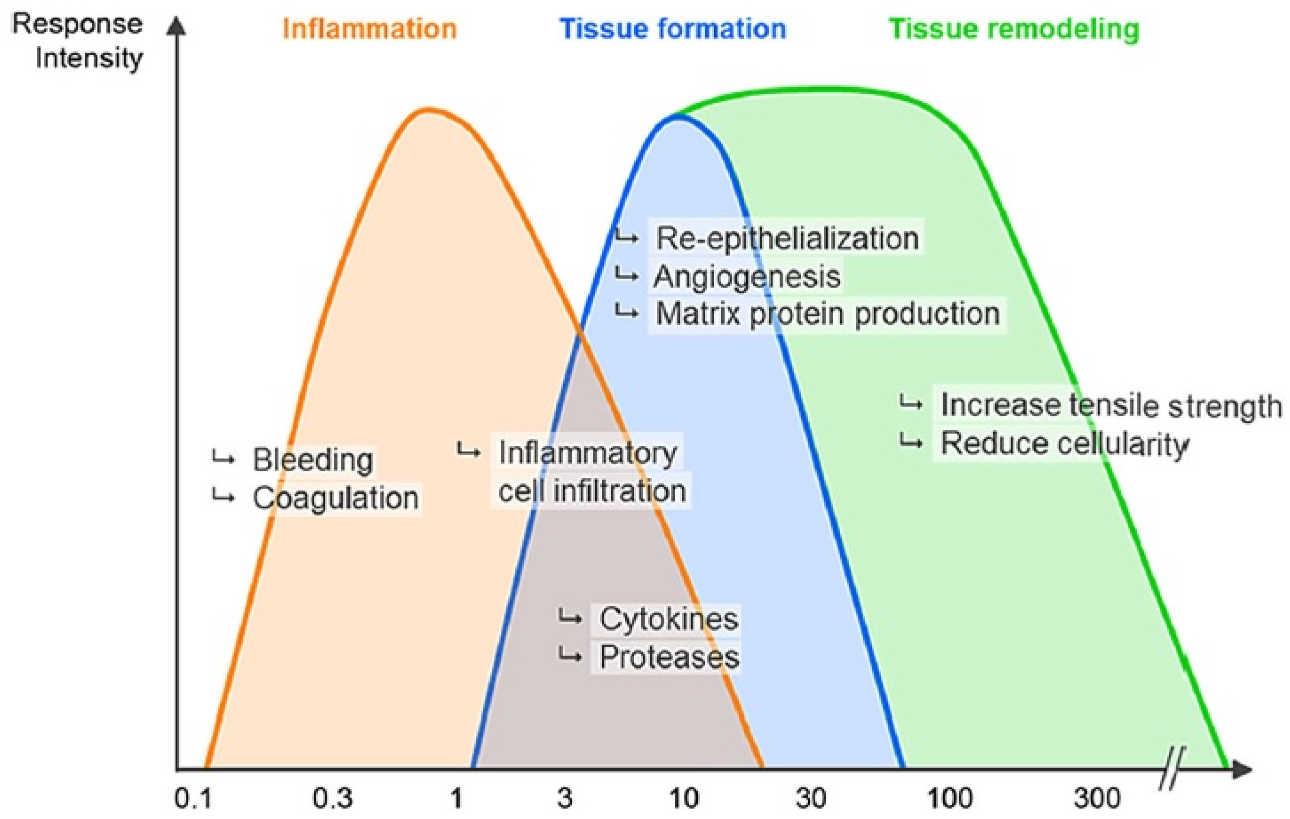

Figure 1: *Wound healing phases (days: log scale). Reference: Rittié (2016).*

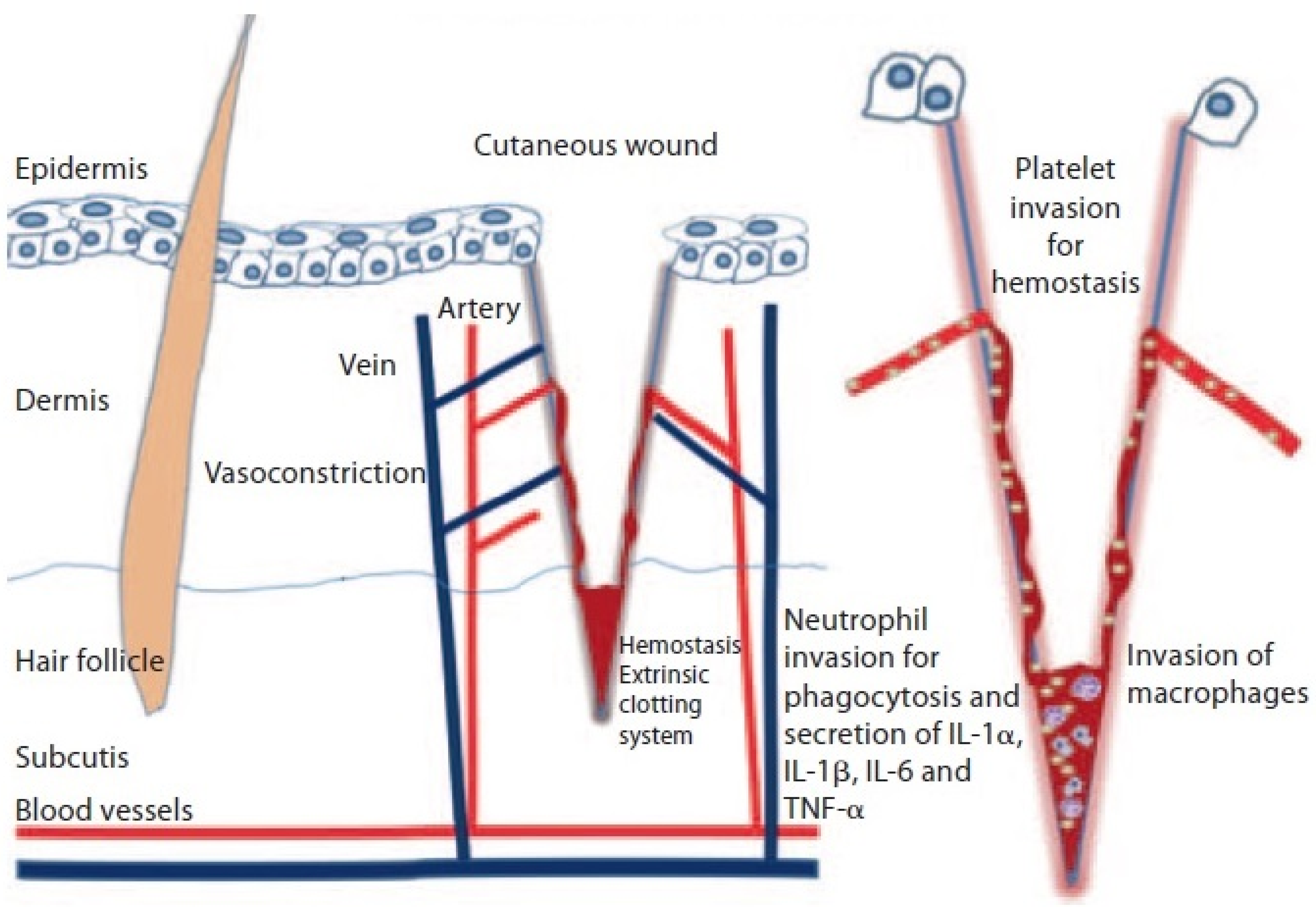

Figure 2: *Inflammatory phase: days 1-3. Reference: Reinke and Sorg (2012).*

The biological experiments was made considering: Lanette cream (LC) and *Copaifera langsdorffii* oleoresin (OR 10%), both of them applied on the dorsal skin of the rats [2]. Biological results are illustrated in the Figure 3 and Figure 4, respectively.

Figure 3: *Rats lesion pictures treated with LC at 3, 7 and 14 experimentation days, respectively. Reference: Gushiken (2017).*

Figure 4: *Rats lesion pictures treated with OR 10% at 3, 7 and 14 experimentation days, respectively. Reference: Gushiken (2017).*

2. Mathematical Model and Results

We consider two populations of neutrophils, the population of macrophages, a proinflammatory cytokine - interleukin 6 (IL-6), and their interactions. The variables and the parameters description, with their units of measurement, are given in Table 1. According to [1] this process can be modelled by the system of ordinary differential equation (ODE):

$$
\begin{cases}
\dfrac{dn}{dt} &= c - \nu\, n,\\
\dfrac{da}{dt} &= \nu\, n - \gamma_a\, a - \phi\, m\, a,\\
\dfrac{dm}{dt} &= c - \gamma_m\, m,\\
\dfrac{dc}{dt} &= \alpha\, f(t) + \gamma_a \left(\dfrac{a^2}{\beta_a^2 + a^2}\right) - c.
\end{cases}
$$

Table 1: *Variables and the parameters used in the mathematical model [1].*

Variable	Description	Unit
t	Time	day
n	Density of active neutrophils	cell mm^{-3}
a	Density of apoptotic neutrophils	cell mm^{-3}
m	Density of active macrophages	cell mm^{-3}
c	Concentration of Cytokine IL-6 (pro-inflammatory mediator)	pg mm^{-3}
Parameter	**Definition**	**Unit**
χ_n	Maximal rate of neutrophils influx	cell pg^{-1} day^{-1}
χ_m	Maximal rate of macrophage influx	cell pg^{-1} day^{-1}
ν	Rate of neutrophils apoptosis	day^{-1}
ϕ	Rate at which macrophages engulf neutrophils	cell^{-1} mm^{-3} day^{-1}
γ_a	Rate of secondary necrosis	day^{-1}
γ_m	Rate that macrophages leave the tissue	day^{-1}
γ_c	Rate of decay of mediator c	day^{-1}
α	Rate of production of mediator c from initial damage	pg mm^{-3} day^{-1}
k_a	Concentration of (c) produced in response to damage	pg mm^{-3}
β_a	Saturation constant	cell mm^{-3}

The results are illustrated in the Figures 5-8.

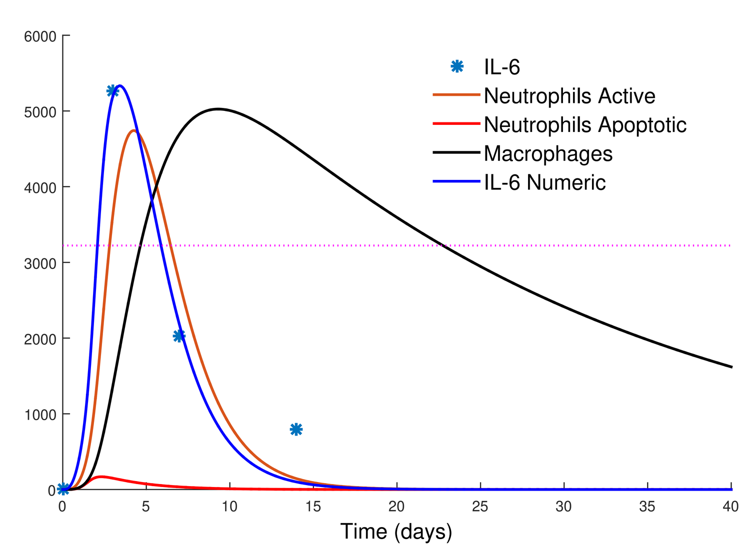

Figure 5: *Healed skin: Lanette cream.*

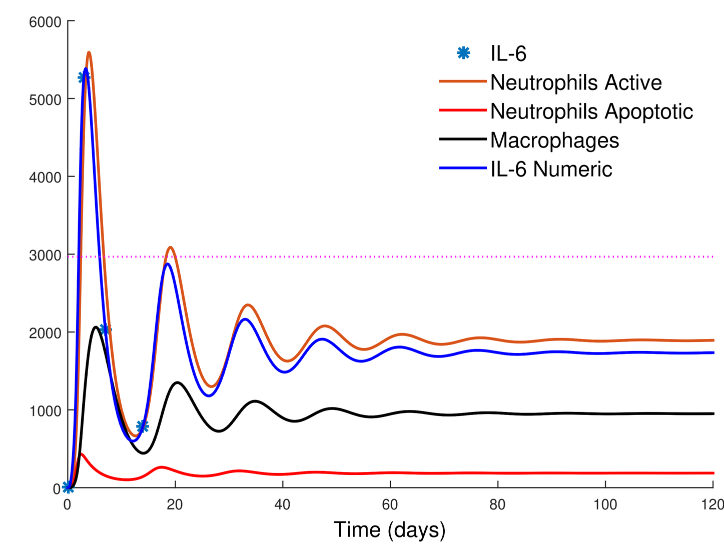

Figure 6: *Unhealed skin: Lanette cream.*

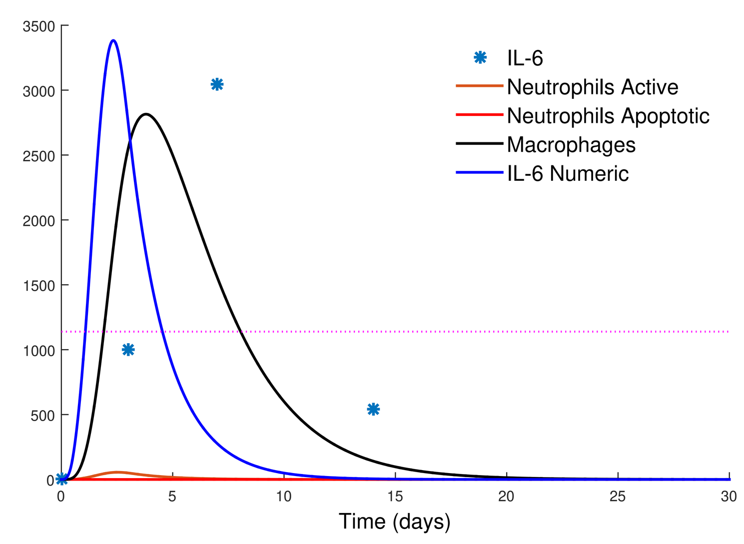

Figure 7: *Healed skin: Oleoresin 10%.*

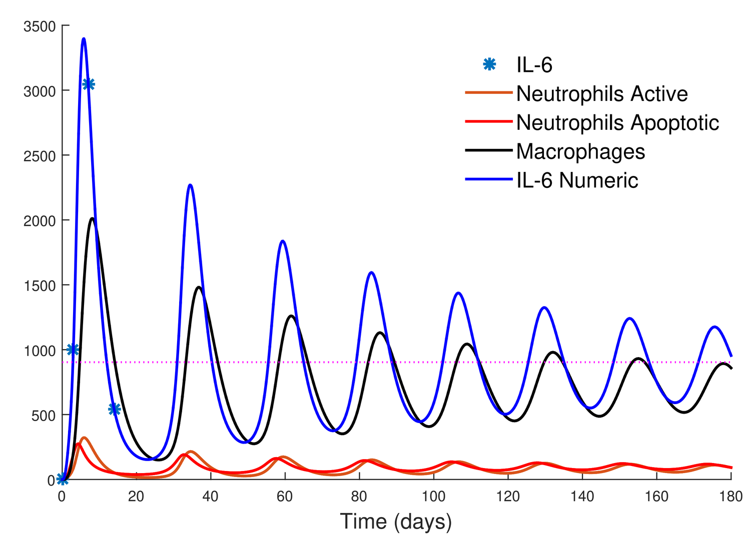

Figure 8: *Unhealed skin: Oleoresin 10%.*

3. Conclusions

The model solution reproduced the dynamics of the neutrophils and macrophages during inflammatory phase nevertheless couldn't find the cicatrization time found in biological experiments. Then it is necessary to improve the model.

Agradecimentos: Partially supported by CAPES-Coordination of Superior Level Staff Improvement and FAPESP, processes: 2011/13630-7 and 2014/23684-5

References

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[2] Gushiken, L. F. S. et al. *Skin wound healing potential and mechanisms of the hydroalcoholic extract of leaves and oleoresin of Copaifera langsdorffii Desf. Kuntze in rats*, Evidence-Based Complementary and Alternative Medicine, (2017), **2017**:1–16 pp.

XI Congreso Latinoamericano de Biología Matemática, 22-25 de Octubre de 2019, Talca, Chile.