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MECHANISM OF WOUND HEALING ACCELERATION BY CHITIN AND CHITOSAN

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Chitin and chitosan exhibit various biological activities and have been used in agriculture, industry, and medicine. Chitin is a neutral (1-4)-linked polysaccharide and a natural mucopolysaccharide that consists of 2-acetamide-2-deoxy-β-D-glucopyranose residues (N-acetyl-D-glucosamine units). It was first described in 1811 by Brancon-not. Chitin is found widely in nature as the skeletal materials of crustaceans and insects, and as a component of the cell walls of bacteria and fungi. It is not soluble in water due to its rigid crystalline structure and intra- and inter-molecular hydrogen bonds. Chitosan is a polymer of D-glucosamine that was discovered by Rouget in 1859. It makes up the cell wall of *Mucor rouxii* and is easily obtained by deacetylation of chitin. Chitosan is readily souluble in water as a result of salt formation by the C-2 amino group of its glucosamine residue with various acids. In rats and rabbits, chitin has been found to increase the tensile strength of sutured wound, which indicates that unmodified chitin can accelerate wound healing. In the case of chitosan, acceleration of wound healing in small animals such as rats and dogs has been well documented in some experimental studies. For example, chitosan has been used to treat burns in rats, and as a hemostatic agent for vascular grafts or for skin and bone wound repair in dogs. These findings strongly suggest that chitin and chitosan may be excellent potential biomaterials, and many attempts have been made to develop chitin and chitosan biomaterials. For several years, we have applied wound healing materials derived from chitin and chitosan in the treatment of companion animals, large domestic animals, and zoo animals, and have demonstrated a positive effect on various types of infected wounds, as well as investigating the histological response *in vivo*, and the influence on inflammatory cells *in vitro*. We have also investigated the mechanisms of wound healing acceleration by chitin and chitosan with reference to the activation and accumulation of polymorphonuclear cells (PMN). These phenomena are induced by complement activation through the alternative pathway. In this pathway, a high level of anaphylatoxins (C3a and C5a) will be produced, and activate endothelium, PMN and mononuclear cells (MN). Therefore, PMN and MN migration is promoted immediately after application of chitin and chitosan to a wound. The PMN, MN and activated complement degrade chitin and chitosan to form oligomers and monomers. These low molecular weight components no longer activate complement, but have a

stronger ability to promote cellular migration than the original polymers.

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