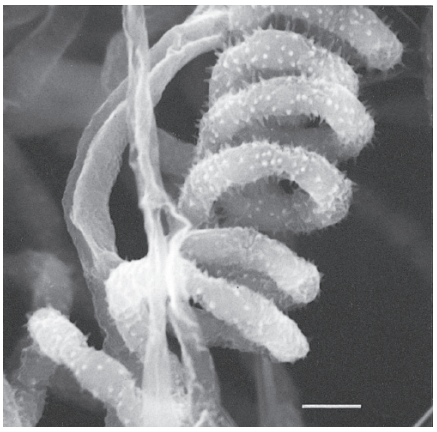
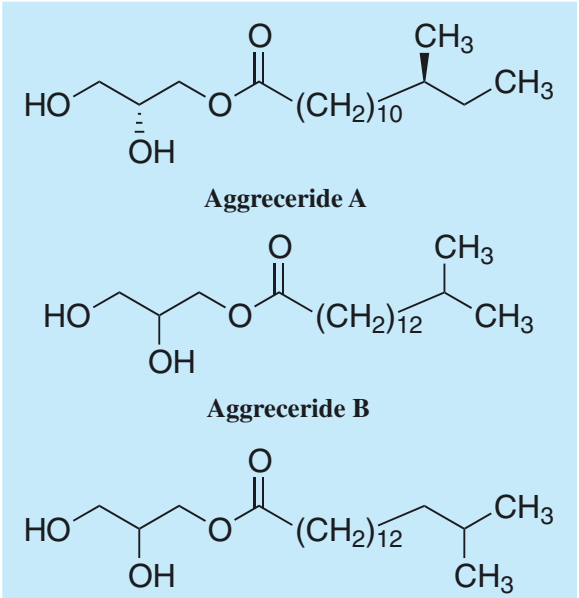
Aggreceride

1. Discovery, producing organism and structures[1)]

Aggrecerides were isolated from the culture broth of the actinomycete strain OM-3209 and identified as inhibitors of platelet aggregation. The absolute configuration and the first total synthesis of aggreceride A was reported by Kitahara *et al*.[2)] (See Appendix-I)



Streptomyces sp. OM-3209



2. Physical data (Aggreceride A)

White powder. $C_{18}H_{36}O_4$; mol wt 316. Sol. in acetone, MeOH, $CHCl_3$. Insol. in H_2O.

3. Biological activity[1)]

Aggreceride A showed inhibitory activity against platelet aggregation induced by thrombin, ADP, arachidonic acid and PAF (platelet activating factor), but was less active against aggregation induced by collagen. Similar inhibitory effects were also observed for components B and C.

Inhibitory effect of aggreceride A on thrombin-induced platelet aggregation

Aggreceride A (μg/ml)	Inhibitory activity (%)
25	81
50	92

Platelet aggregation was induced by thrombin (2 U/ml). The degree of aggregation was measured by visual inspection.

Aggreceride A inhibited thrombin-induced MDA (malondialdehyde) formation, suggesting that the target of aggreceride A was at or lower than the level of arachidonic acid metabolism.

Aggrecerides show no antimicrobial activity at a concentration of 1 mg/ml using the paper disc method against yeast, fungi or bacteria. The acute toxicity (LD_{50}) of aggrecerides in mice was >200 mg/kg (i.v.).

4. References

1. [344] S. Ōmura *et al*., *J. Antibiot*. **39**, 1180-1181 (1986)
2. T. Kitahara *et al*., *Biosci. Biotech. Biochem*. **59**, 78-82 (1995)