FERTILITY REGULATING ACTIVITIES OF SOME SELECTED SRI LANKAN MARINE RED ALGAE

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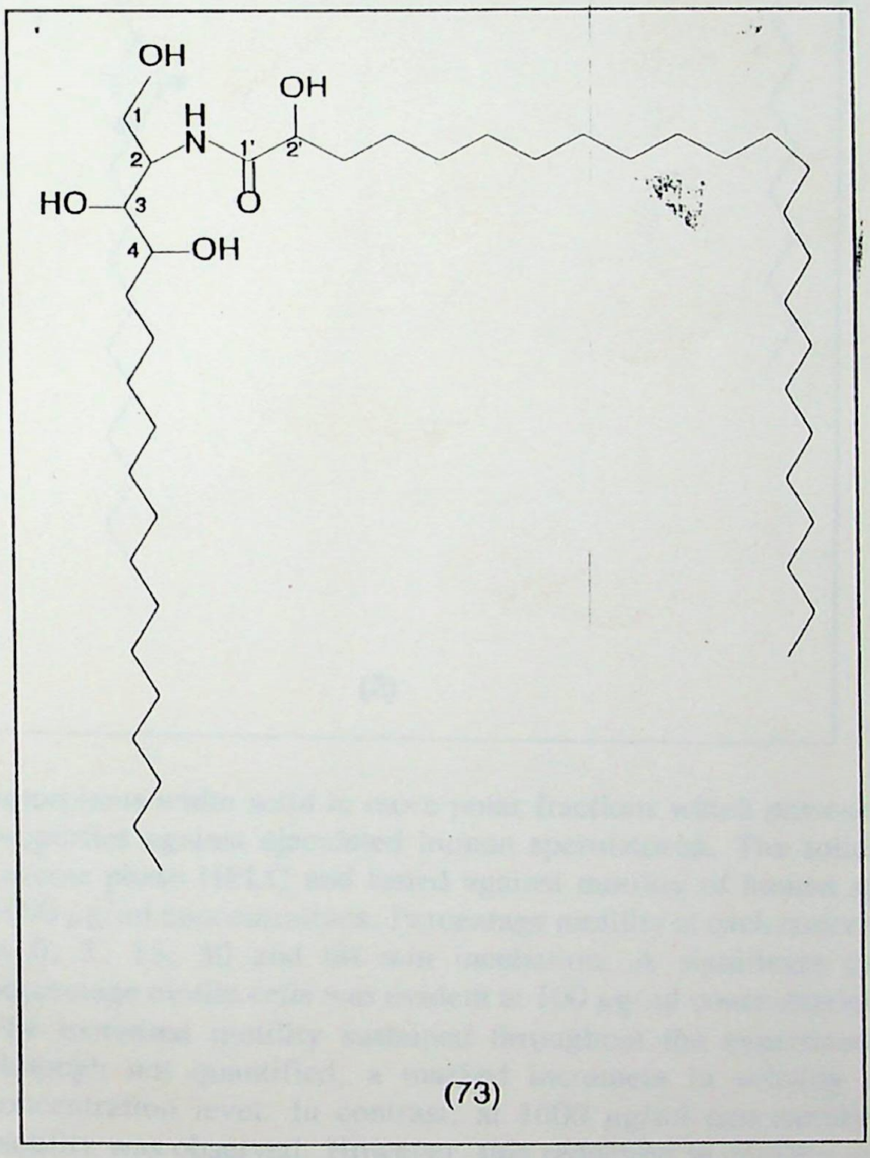
Abstract

Five different varieties of marine red algae : *Gelidiella acerosa*, *Gracilaria corticata*, *Gelidium crinale*, *Jania* sp. and *Gracilaria* sp3, were collected from coastal waters of Southern Sri Lanka and extracted with 1:1 methanol- methylene chloride. Resulting crude extracts (CE), those which had a yield of > 2 g/kg : *Gracilaria corticata*, *Gelidiella acerosa* and *Jania* sp were coprecipitated with polyvinylpyrrolidone and tested for post coital contraceptive activity in pregnant rats at doses of 500 and 1000 mg/kg/ml/day through oral intubation from day 1 to day 7 of pregnancy.



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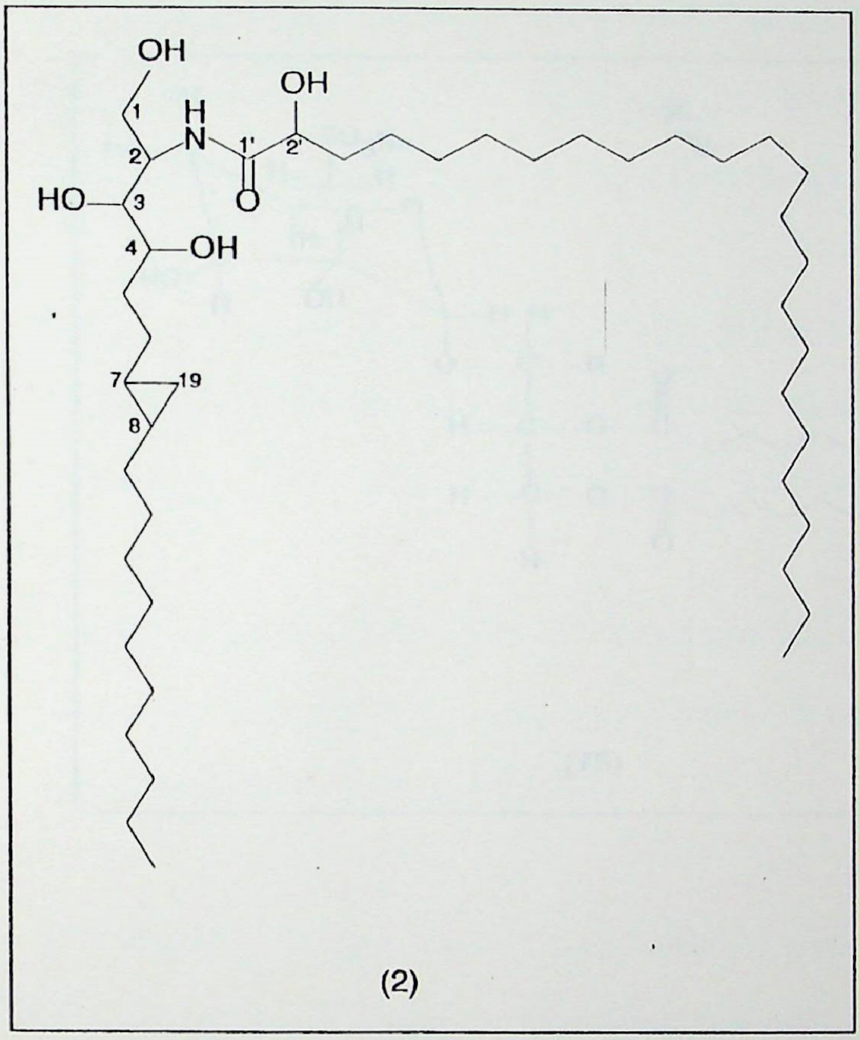
Crude extract of *Jania* sp. had no post-coital contraceptive activity in rats. In contrast, the animals treated with CE of *Gracilaria corticata* showed a significant ($p < 0.05$) pre-implantation loss ($49.57 \pm 10.46\%$) at 1000 mg/kg/ml dose level. On the other hand, animals treated with CE of *Gelidiella acerosa* had a significant post-implantation loss both at 500 and 1000 mg/kg/ml dose levels (500 mg/kg/ml dose: $43.75 \pm 18.57\%$; 1000 mg/kg/ml dose: 100%).

Studies on the mechanism /s of action of the CE of *G. acerosa* revealed that the contragestive effect of *G.acerosa* was not associated with oestrogenic or anti-oestrogenic activity, but mediated via an anti-progesterone mechanism. Furthermore, the anti-progesterone activity of CE of *G. acerosa* appears to be mediated via a mechanism other than progesterone receptor antagonism, probably involving progesterone synthesis or release in the corpus luteum.

The active component of the CE of *G. acerosa* was separated through six chromatographic steps and identified through extensive spectroscopic analysis as N-2'-hydroxy-lignoceroyl- 2-amino-1,3,4-trihydroxy-octadecane (73).



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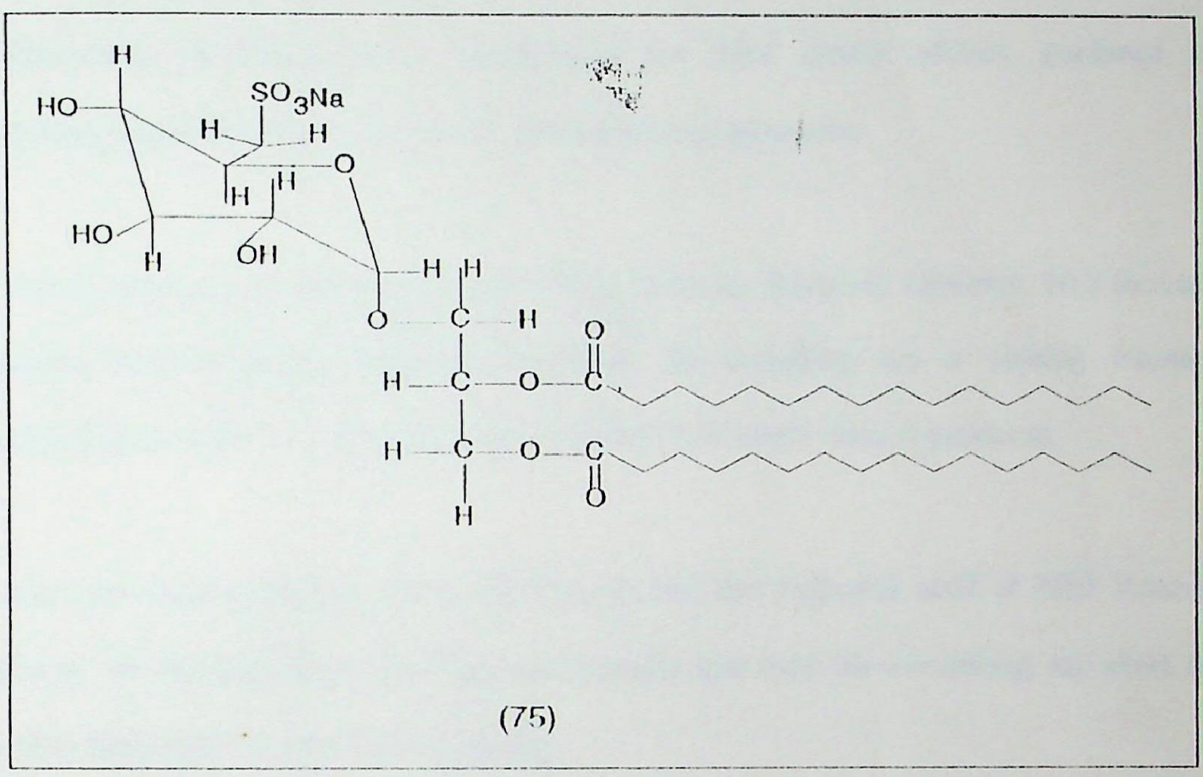
Further analysis of the spectral data revealed that 20% of the active compound possesses a cyclopropane ring in one of the two alkyl chains and this second compound was identified as N-2'-hydroxy-lignoceroyl-2-amino-1,3,4-trihydroxy-(7-8)19-cyclo-octadecane (74).

The active compound showed 80% contragestive activity in pregnant rats at 6.0 mg/kg/ml concentration. In a separate study, the active component showed 26.89% inhibition in platelet activating factor induced human platelet aggregation at 41.6 μg/ml concentration level.

Fractionation of CE of *G.acerosa* resulted with an amorphous white solid in more polar fractions which possess sperm motility stimulating properties against ejaculated human spermatozoa. The solid was further purified over reverse phase HPLC and tested against motility of human spermatozoa at 10, 100 and 1000 μg/ml concentrations. Percentage motility at each concentration levels was recorded at 0, 5, 15, 30 and 60 min incubation. A significant ($p < 0.05$) increment in the percentage motile cells was evident at 100 μg/ml concentration after 5 min of incubation. The increased motility sustained throughout the experimental period. Furthermore, although not quantified, a marked increment in velocity was also observed at this concentration level. In contrast, at 1000 μg/ml concentration, a marked reduction in motility was observed. However, this reduction in motility at 1000 μg/ml concentration was not statistically significant ($p > 0.05$). A reduction in velocity was also evident at this concentration level. However, 10 μg/ml concentration had no effect either on the percentage motility or velocity of spermatozoa.

This sperm stimulating compound was subjected to extensive spectroscopic analysis and the compound was identified as 2',3'-di-O-(Pentadecanoyl)-glyceryl-6-sulfo-α-D-quinovopyranoside (75).



(75)

The effect of this compound on motility of spermatozoa was dose dependent and had a bell shape distribution for the effect on % motility against doses tested. Thus, the motility stimulating property appears to be receptor mediated. Since the compound is a sulfated glycoconjugate, the probable mechanism of this sperm stimulation was proposed to be mediated via stimulating intracellular alkalinization, Ca^{++} uptake, adenylate cyclase activity and elevation in cAMP concentration as do other sulfated glycoconjugates so far tested.

This study reports three new compounds. In addition, this study for the first time reports contraceptive property of sphingosine derivatives and sperm stimulating potential of sodium sulfonate glycolipids. These findings indicate that marine red algae is a useful source to be harvested for potential post coital contraceptive drugs and sperm stimulants.