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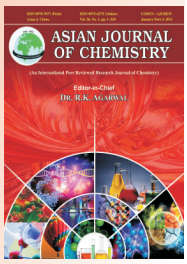

NOTE

Phytol May Inspire New Medicinal Foods for the Treatment of Heart Disease

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This study aimed to investigate *in vitro* antibacterial activity of phytol against the selected Gram positive bacteria (*Clostridium sporogenes*, *Enterococcus faecalis* and *Sarcina lutea*) involved in the pathogenesis of infective endocarditis. The examined natural product has proved to be active against all the tested bacteria, but to a varying degree. Indeed, phytol inhibited *E. faecalis* growth (MIC 1.56 ± 0.04 µg/mL) more effectively than gentamycin and ampicillin (MIC 5.00 ± 0.06 and 16.00 ± 0.03 µg/mL, respectively). Both its freely presence in nutrition and easy availability support the development of a new phytol based medicinal foods targeting heart disease.

Keywords: Diterpene alcohol, Antibacterial activity, *Enterococcus faecalis*, Infective endocarditis.

Traditional Chinese medicine suggests that some mosses of the genus *Rhodobryum* (Bryaceae) can be used as crude drugs for heart disease[1]. Actually, this genus includes four species present in northern hemisphere[2] together with some additional ones from subtropical or tropical regions[3]. The moss *Rhodobryum ontariense* has a wide but very fragmented distribution[4]. Preliminary analysis of its volatiles has indicated phytol as the main constituent (31.95 %)[5]. Such abundance of this natural product has not previously been reported in essential oils of other mosses[6].

Phytol (3,7,11,15-tetramethyl-2-hexadecen-l-ol) is an acyclic monounsaturated diterpene alcohol, present in vitamin K, vitamin E and other tocopherols. It is an active ingredient in formulations that lower serum levels of triglycerides and/or cholesterol[7]. Indeed, this compound may be administered both to patients (*e.g.* with type II diabetes, obesity or heart disease) and healthy individuals[8].

A large body of evidence implicates number of microbial strains in the pathogenesis of infective endocarditis (IE)[9,10]. Enterococci are the third most common etiologic agent of IE worldwide after *Staphylococci* and *Streptococci* being responsible for 10 to 15 % of cases[11]. Approximately 90 % of the enterococcal endocarditis cases are caused by *Enterococcus faecalis*, with < 5 % by E. faecium. The bacteria *Clostridium sporogenes* and *Sarcina lutea* are also listed among the microorganisms which might provoke IE[12,13].

The aim of this study was to investigate *in vitro* antibacterial activity of phytol against three IE bacteria for the first time.

The examined chemical was used as received from Sigma-Aldrich, Munich, Germany (97 %, mixture of isomers), without any further purification. The Gram-positive bacteria *Clostridium sporogenes* ATCC 19404, *Enterococcus faecalis* ATCC 19433 and *Sarcina lutea* ATCC 9341 were obtained from the Mycological Laboratory, Faculty of Sciences, University of Novi Sad, Novi Sad, Serbia. The antibacterial assay was carried out by a 96 well microdilution method[14]. Gentamycin (Sigma-Aldrich, Munich, Germany) and ampicillin (Panfarma, Belgrade, Serbia) were used as a positive control, respectively. All experiments were performed in duplicate and repeated three times.

Phytol has showed to be active against all the tested bacteria, with MIC and MBC values 1.56-6.25 and > 12 µg/mL, respectively (Table-1).

The most susceptible bacterium was *E. faecalis*. Actually, this organic compound inhibited *E. faecalis* growth more effectively (MIC < 2 µg/mL) than gentamycin and ampicillin (MIC 5 and 16 µg/mL, respectively). The reports on phytol antibacterial activity are relatively scarce. Rajab *et al.*[15] reported a MIC value of 2 µg/mL against the IE bacterium *Mycobacterium tuberculosis* for (*E*)-phytol, (*Z*)-phytol, commercially available 2:1 mixture of (*E*) and (*Z*)-phytol and (3*R*,*S*,7*R*,11*R*)-

TABLE-1
MINIMUM INHIBITORY (MIC) AND BACTERICIDAL (MBC) CONCENTRATIONS OF PHYTOL

Bacteria	Phytol[*¥]	Gentamicin[*#¥]	Ampicillin[*#¥]
Clostridium sporogenes ATCC 19404	3.12 ± 0.08 / >12	2.50 ± 0.02 / > 20	64.00 ± 0.06 / > 128
Enterococcus faecalis ATCC 19433	1.56 ± 0.04 / > 12	5.00 ± 0.06 / > 20	16.00 ± 0.03 / > 128
Sarcina lutea ATCC 9341	6.25 ± 0.06 / > 12	2.50 ± 0.03 / > 20	2.00 ± 0.03 / > 2

[*]MIC/MBC (µg/mL); [#]Positive control; [¥]$p < 0.05$

phytanol, respectively. Furthermore, the derivatives (*E*)-phytol acetate, a mixture of the (2*S*,3*S*)- and (2*R*,3*R*)-isomers of (*E*)-phytol epoxide and (3*R*,*S*,7*R*,11*R*)-phytanic acid displayed lower activities with MICs of 8, 16 and > 128 µg/mL, respectively[15]. On the other hand, Pejin *et al.*[16] reported a MIC value of 3 µg/mL against the IE bacterium *Listeria monocytogenes* for the phytol sample screened herein.

Phytol is a common and nonmutagenic food additive, with satisfactory safety. In addition, it is structurally simple, easily available and cost-effective chemical[17]. The low toxicity and high tolerance by mammals make this terpene molecule good candidate for the key ingredient of a new medicinal foods targeting heart disease.

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