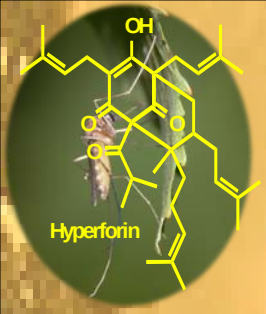
HYPERFORIN AND DEOXYCOHUMULONE AS POTENTIAL LARVICIDAL MOSQUITO AGENTS



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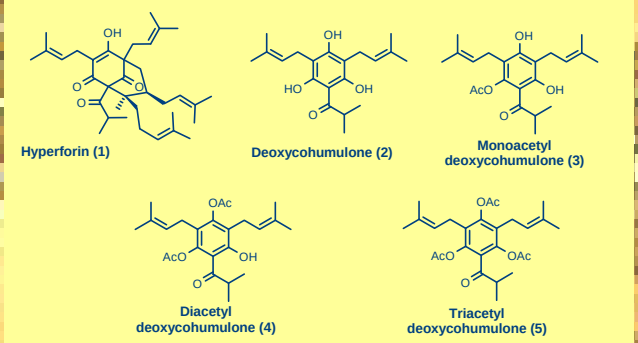
INTRODUCTION

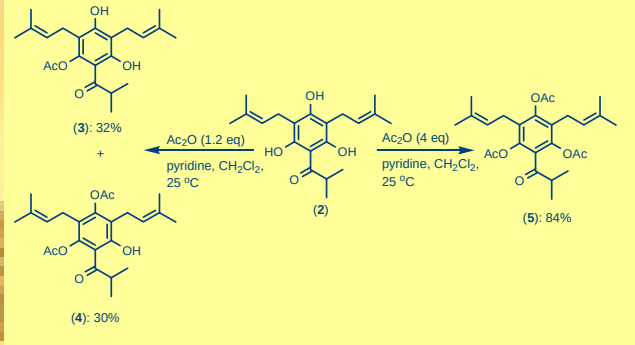
Hyperforin is a polycyclic polyprenylated acylphloroglucinol, a bioactive compound with fascinated chemical structure and intriguing biological activities. Hyperforin (**1**) belongs to the family of Clusiaceae and has been isolated from *Hypericum perforatum* (St. John's wort) (Gurevich et al. 1971). Hyperforin, biosynthetically derives from deoxycohumulone (**2**). The Ancient Greeks were familiar with the therapeutics properties of the *Hypericum perforatum* extract as an antidepressant agent or as wound healing. Hyperforin, is mainly responsible for the activities of *Hypericum perforatum*, concerning the treatment of depression, anxiety, schizophrenia and cancer (Grossman et al. 2003; Medina et al. 2006).

Main objective of this study was the evaluation of the larvicidal activity of hyperforin (**1**) and its bioprecursor, deoxycohumulone (**2**) against *Cx. pipiens* (Scheme 1). Synthesis and examination of the relation between chemical structure and effectiveness of three new acetylated deoxycohumulone derivatives: monoacetyl deoxycohumulone (**3**), diacetyl deoxycohumulone (**4**) and triacetyl deoxycohumulone (**5**) (Scheme 2,3) were also investigated.

Scheme 1: Structures of hyperforin, deoxycohumulone, monoacetyl deoxycohumulone, diacetyl deoxycohumulone and triacetyl deoxycohumulone.



Scheme 2: Acetylation control of deoxycohumulone.



MATERIALS AND METHODS

All experiments for the extraction and the isolation of hyperforin from *Hypericum perforatum*, were carried out according to Adam Petra (Adam et al. 2002). The larval mortality bioassays were carried out according to the test method of larval susceptibility as suggested by the World Health Organization (WHO 1981). The colony of the species *Cx. pipiens* biotype *molestus* has been maintained in the laboratory of Benaki Phytopathological Institute, Kifissia.

Table 1: Larvicidal activities against *Cx. pipiens* of compounds (1) – (5).

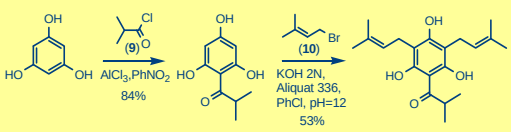
Compound	LC_{50} (95% CL)[a]	LC_{90} (95% CL)[a]	Slope (±SE)	x^2
Hyperforin (1)	43.87 (36.61-50.99)	130.33 (108.51-166.85)	2.71±0.28	11.41
Deoxycohumulone (2)	51.03 (40.95-60.73)	118.34 (96.7-159.99)	3.5±0.34 [b]	23.27
Monoacetyl deoxycohumulone (3)	135.92 (124.29-149.37)	245.01 (212.11-304.28)	5.0±0.44	30.03
Diacetyl deoxycohumulone (4)	>300	–	–	–
Triacetyl deoxycohumulone (5)	>300	–	–	–

[a] LC values are expressed in mg/L and they are considered significantly different when 95% CL fail to overlap
[b] Since goodness–of–fit test is significant (P<0.05), a heterogeneity factor is used in the calculation of confidence limits (CL)

RESULTS

The larval mortality bioassays revealed that hyperforin (**1**) and deoxycohumulone (**2**) were very effective (LD_{50} = 43.87 and 51.03 mg/L, respectively) while the presence of one or more acetates decreases molecule's activity. As a result the mono acetyl deoxycohumulone analogue (**3**) was less effective (LD_{50} = 135.92mg/L) and the other two acetylated analogues (**4**) and (**5**) were inactive (LD_{50} >300mg/L) (Table 1). Our study revealed that the presence of one or more acetates block molecule's activity.

Scheme 3: Synthesis of deoxycohumulone.



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Acknowledgments

This research has been co-financed by the European Union (European Social Fund – ESF) and Greek national funds through the Operational Program "Education and Lifelong Learning" of the National Strategic Reference Framework (NSRF) - Research Funding Program: Heracleitus II. Investing in knowledge society through the European Social Fund.