



Thymus vulgaris essential oil enclosed in β -cyclodextrin as drug delivery system: a promising alternative for antibiotic usage in combating *Salmonella*

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Abstract

The essential oil of *Thymus vulgaris* (TVEO) has been used in traditional medicine for centuries. However, its low solubility and high volatility have limited its usage. In this study, TVEO was extracted, and its chemical composition was identified. The TVEO was extracted using a Clevenger-type apparatus and identified using Gas Chromatography/Mass Spectrometry (GC/MS). An inclusion complex was then formulated with β -cyclodextrin (β CD) to enhance its solubility, and the antibacterial activity was tested against 14 multidrug-resistant bacteria. When treated with the complex, the inactivation kinetics of *Salmonella typhimurium* were evaluated under simulated intestinal conditions. Thymol and carvacrol were identified as the significant components of TVEO, comprising 47.53% and 19.27% of the oil, respectively. The solubility diagram of enclosed Thymol exhibited a Bs-type profile, with an association constant (K_s) of 202.35 M^{-1} and a complexation efficiency of 55.07% for the formulated complex TVEO- β CD. The antibacterial activity demonstrated significant inhibition against all tested strains except for three. The study demonstrates the effectiveness of the TVEO- β -CD complex against *S. typhimurium* in intestinal conditions, a novel application. Unlike prior research, our work focuses on this complex's efficacy, specifically against *Salmonella*, showing prolonged inhibitory effects. This reveals the enhanced antibacterial activity of β -CD in solubilising TVEO, offering potential as an antimicrobial agent.

Keywords *Thymus vulgaris* essential oil · β -cyclodextrin · Inclusion complex · Antibacterial effect · Simulated intestinal conditions

Introduction

In recent years, herbal products have increased in popularity due to increased awareness of the benefits of natural health-care and alternative therapy methods. One medicinal plant that has gained widespread recognition is *Thymus vulgaris*, also known as common thyme.

Multiple studies have been conducted on *T. vulgaris* essential oil to assess its chemical composition and various properties, including antibacterial (Nadia and Rachid 2013), antioxidant (Ismaili et al. 2017), anti-inflammatory (Abdelli et al. 2017), antiseptic, and analgesic effects (Parsaei et al. 2016; Rašković et al. 2021). The chemical profile of the oil often reveals the presence of monoterpene alcohols such as carvacrol and Thymol. However, this composition can vary based on factors such as climate, soil composition, extraction methods, origin, and harvest time of the plant (Lemos et al. 2017; Nezhadali et al. 2014). Nonetheless, most studies support the efficacy of *T. vulgaris* for these properties. Despite its potential, the low solubility, high volatility, and rapid oxidation of its essential oil in the presence of oxygen have limited its effectiveness and application (Capelezzo et al. 2018), as well as its bioavailability in vivo (Nieddu et al. 2014).

Some studies have attempted to form an inclusion complex of *T. vulgaris* essential oil (TVEO) or one of its major

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