

Research Article

Study on the Structural and Physicochemical Characteristics of Newly Synthesized Compounds Based on Menthol-Derived Amino Acids

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Abstract

This article discusses the optimized conditions for synthesizing novel menthol derivatives through its interaction with selected amino acids. This study presents the optimized conditions for synthesizing novel menthol derivatives through reactions with selected amino acids. The resulting compounds were characterized to determine their physicochemical properties, including appearance, aggregate state, and melting point. Notable variations in these characteristics suggest distinct structural and thermal behaviors among the synthesized derivatives. These findings imply potential applications in pharmaceuticals, materials science, and other related fields. The physical constants of the new compounds were determined, and their structures were analyzed using infrared (IR) and mass spectrometry. In the IR spectra of the complex esters, the absence of the hydroxyl (-OH) stretching vibration near 3245 cm^{-1} confirms ester formation between the hydroxyl group of menthol and the amino acid moieties. These spectral features support the successful synthesis of complex esters and highlight the interaction mechanism. This work contributes to the development of functionalized organic molecules with promising physicochemical and possibly biological properties.

Keywords

Menthol, Serine, Proline, Lysine, Physical Chemical Constants, IR Spectrum Phenylalanine Instruction

1. Introduction

Nowadays, the use of natural products, particularly those derived from plants, is gaining increasing importance in the extraction of biologically active substances from medicinal plants and the development of alternative production methods. The ineffectiveness of traditional medicines, the misuse of synthetic drugs, and issues related to side effects and toxicity have heightened interest in plant-based medicines. This has led to a growing focus on studying the composition of medicinal plants, isolating natural biologically active compounds, analyzing their properties, and exploring their applications in

medicine. In this context, our research is centered on investigating the biological activity and structure of new compounds derived from menthol, a substance commonly found in the mint plant.

Plants remain the main source of pharmaceuticals even after several inventions in industrial development and organic chemistry industry. According to the World Health Organization, 80% of people around the world use traditional medicine and treatment methods to improve their health [1]. In the modern days, the natural resources of the medicine supplied

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worldwide are about 25%. According to WHO research, 11% of them are synthetic drugs made from only plant sources and the majority are made from natural plants [2]. Natural chemicals naturally help to rationally design and develop innovative pharmaceutical products, to identify previously undiscovered medicinal properties. Recently the use of natural products, especially those derived from plants for medical purposes and alternative therapies has shown its importance. Problems related to ineffectiveness traditional medicines, misuse of synthetic drugs, side effects and toxicity have generated interest in plant-based medicines [3-5].

Conventional new drug development is a relatively cost-effective, risky process involving target selection and screening and search and optimization of harmful compounds [6]. In addition, high failure rates in clinical trials are often associated with factors such as low drug efficacy, low binding strength, off-target effects or physicochemical properties such as stability or solubility, as well as high toxicity and drug pharmacokinetics [7, 8]. In vivo and in vitro methods have been commonly used to assess drug safety, including adverse effects and toxicity, but these methods are time-consuming, labor-intensive and cost-effective, which remains a problem [9]. Due to limitations of results, accuracy, efficiency, and cost, there is increased focus on strategies to develop fast and inexpensive, accurate target detection and prediction methods, which has led to the development of computational techniques that are often used in drug discovery [10, 11].

New drugs can be synthetic, semi-synthetic, plant derived or re-manufactured drugs. If the structure is available, structure-based virtual screening and molecular typing are possible. Finding key therapeutic targets defined as a target or biological entity, usually a protein that can modify disease phenotypes is the first and most important step in the drug development process [12, 13]. The purpose of the current research is to create new compounds of menthol, to study of physicochemical properties of the obtained compound, to analyze its structure, and to determine its biological activity. Menthol is widely used as a chemical compound in perfumery and cosmetics and service as a pharmaceutical adjuvant, food additive and tobacco flavor due to its pleasant smell and cooling effect [14, 15]. The compound is isolated from natural peppermint oil as enantiopure L-menthol or produced by asymmetric synthesis or the Haarmann-Reimer process. Isolation from multicomponent systems by distillation, extraction, or crystallization is a necessary step in any production method [16].

Menthol is isolated from peppermint or other peppermint oils. Chemically, plant is a plant derived cyclic monoterpene alcohol. It is commonly used in oral hygiene pesticides, cosmetics, pharmaceuticals, confectionary products and as a flavoring agent. It has antioxidant, anti-inflammatory and analgesic effects [17, 18]. Medicinal properties are related to the presence of phenolic chemicals in mint species [19, 20]. From this point of view, based on the results of many studies, we synthesized several new derivatives of menthol with amino acids. The hydroxyl group of menthol reacts with the carboxyl group of amino acids such as primary alcohols to form complex esters.

2. Research Methodology

0.013 mol of menthol is taken and dissolved in 0.5 mol of methanol solvent. It is mixed for 30 minutes, 0.01 mol of amino acid is taken and thoroughly dissolved in 5 ml HCl (conc). After both of them are melted, they are poured into one container. The resulting mixture is mixed for 5-6 hours at a temperature of 35-40 °C to obtain compounds of menthol.

Analysis of their chemical structure is extremely important in the study of new compounds derived from menthol and amino acids. Modern analytical methods are widely used to determine the structure and correctly identify each element. Basically, we used methods such as mass spectrometry (MS), infrared spectroscopy (IR), and high-performance liquid chromatography (HPLC) to identify the physical properties and initial structure of the obtained compounds. Techniques such as infrared spectroscopy (IR) and high performance liquid chromatography (HPLC) play an important role study and analysis of those compounds. Using infrared spectroscopy, the functional groups present in the compound are determined. The presence of menthol's phenolic hydroxyl group and other groups derived from amino acids is confirmed by IR spectra.

High performance liquid chromatography was used to purify and separate compounds derived from menthol and amino acids. Purified compounds were analyzed by HPLC, which then allowed for further elucidation of compound structure by methods such as NMR and MS.

These analytical methods help to elucidate the structure of new compounds derived from menthol and amino acids, which is primary importance in evaluating the efficacy and safety of menthol as a drug.

3. Analysis and Results

Table 1. Physicochemical constants of New Derivatives of Menthol with Some Amino Acids.

Nº	Substant	Mr (g/mol)	T _m °C	R _f * System	Solubility	Efficiency %
1	Menthol (M)	C ₁₀ H ₂₀ O 156	42 ± 2	0,3	Ethanol, Acetone, Dioxane, Pyridine	84,6

№	Substant	Mr (g/mol)	T _m °C	R _f * System	Solubility	Efficiency %
2	Mentholprolinate	C ₁₆ H ₂₇ NO ₃ 281,39	50±2	0,35	Ethanol, Hexane, Ethyl Acetate, Chloroform, Benzene	75,2
3	Mentholserinate	C ₁₃ H ₂₃ NO ₃ 241,33	44±2	0,4	Ethanol, Chloroform, Benzene	77,9
4	Mentholleucinate	C ₁₃ H ₃₂ N ₂ O ₃ 300,44	55±2	0,35	Hexane, Ethylacetate, Chloroform, Benzene, Ethanol	80,2

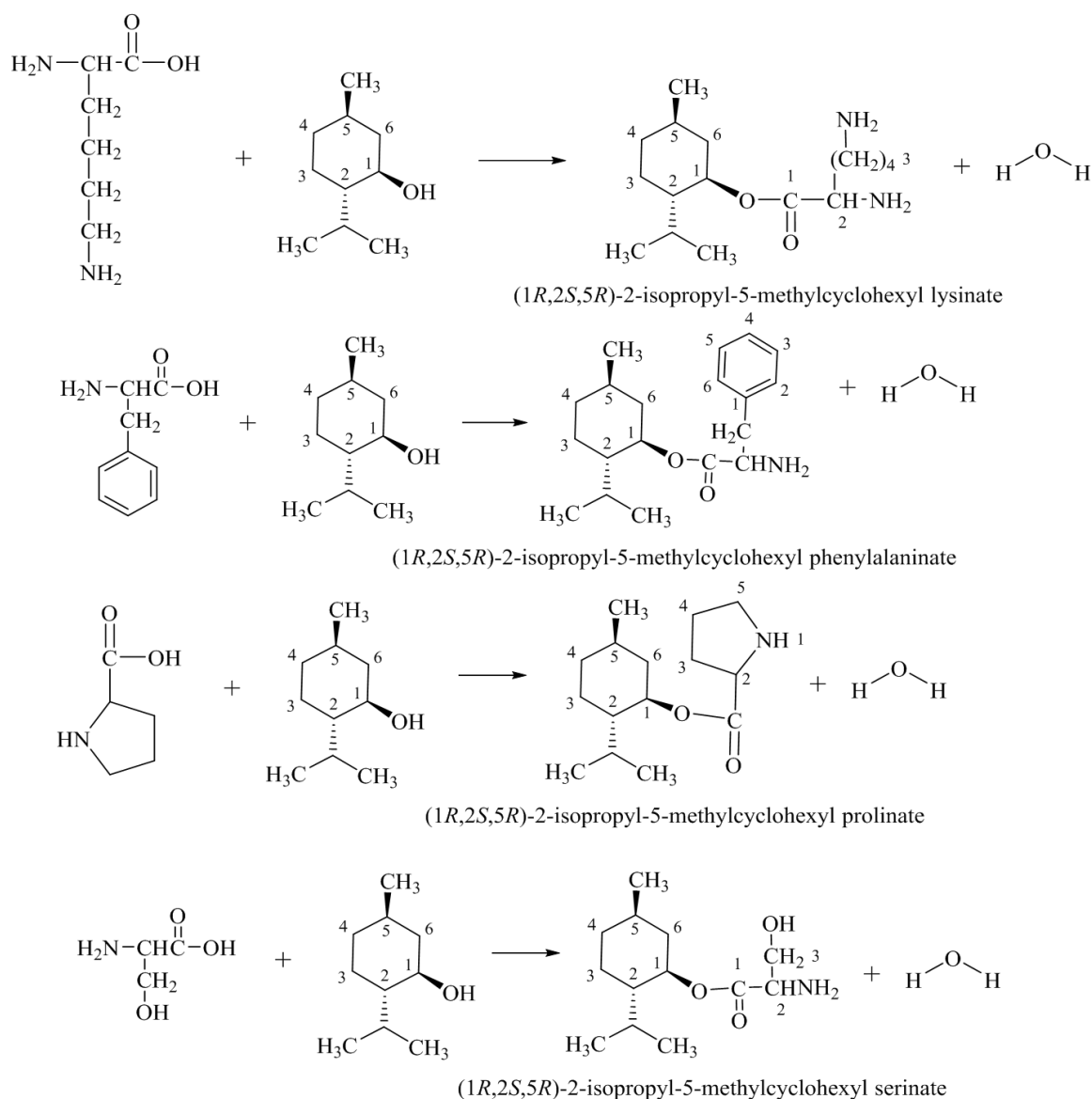


Figure 1. The synthesis of new derivatives of menthol with amino acids was carried out with the following reaction scheme.

In the IR spectrum of derivatives of newly synthesized menthol with amino acids, the valence vibrations of the C=O group of the carbonyl groups are observed in the region of 1730-1710 cm⁻¹, the valence vibrations of the -OH groups of menthol are observed in the region of 3500-3250 cm⁻¹ and belong to them as a result of the replacement of hydroxyl

groups with acetyl groups is explained by the decay of the frequency of vibrations.

The physicochemical constants of the obtained complex ethers were determined, and their structure was confirmed by comparing the IR spectra with the spectrum of the original substances.

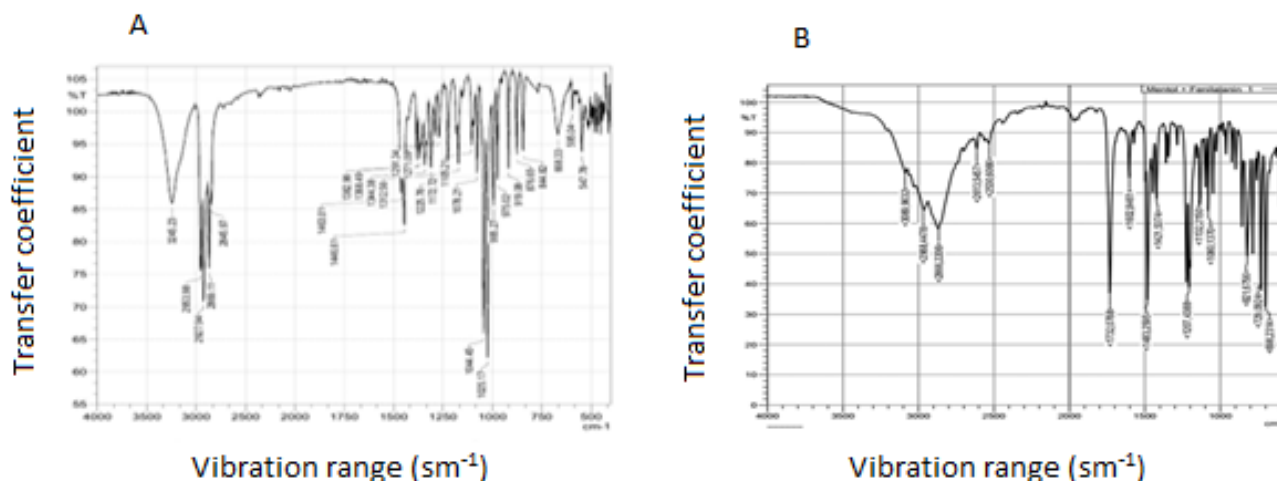


Figure 2. A) IR spectrum of menthol B) IR spectrum of mentholphenylalanine.

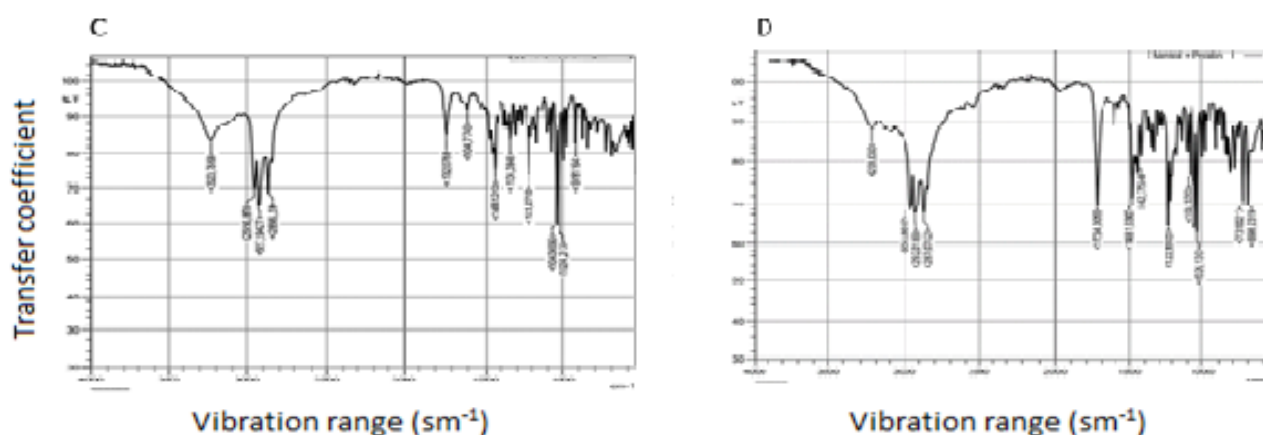


Figure 3. C) IR spectrum of menthollesinate D) IR spectrum of mentholprolinate.

From the IR (infrared) spectrum of menthol presented in Figure 2, we can see that the structure of the menthol molecule is characterized by several main peaks. The chemical formula of menthol is $C_{10}H_{20}O$, which is a cyclic terpene alcohol. The O-H group has a broad peak around $3300-3500\text{ cm}^{-1}$, which indicates the characteristic of the hydroxyl (O-H) group in alcohols.

In the IR spectrum, C-H group has several clear peaks in the range $2800-3000\text{ cm}^{-1}$ due to C-H stretching vibrations of methyl (CH_3), methylene (CH_2) and methine (CH) groups. The C-O group has a C-O stretching vibration in the range of $1000-1300\text{ cm}^{-1}$, which is typical for alcohols. Bending vibrations of CH_3 and CH_2 groups can be seen in the range of $1300-1500\text{ cm}^{-1}$.

IR (infrared) spectroscopic analysis of menthol and leucin combination (picture 3) shows the characteristics of chemical bonds and functional groups between the two components. The main functional group of menthol is -OH (hydroxyl), which has an inverse peak in the IR spectrum between $3300-3500\text{ cm}^{-1}$. Leucine shows significant absorption peaks in the spectrum due to its -COOH (carboxyl) and -NH₂ (amine)

groups.

In the IR spectrum of complex esters, the frequency of the -OH vibration in the region of 3245 cm^{-1} is not observed, which in turn indicates the formation of complex esters between the hydroxyl group of menthol and amino acids.

In the region of 1726 cm^{-1} , the valence vibrations of the -C=O (carbonyl) group are observed in the field of vibration of functional groups.

4. Conclusions and Suggestions

The physical constants of the obtained new compounds were determined, IR and Mass spectra were determined. In the IR spectrum of complex esters, the -OH vibration frequency is not observed in the region of 3245 cm^{-1} , which in turn indicates the formation of complex esters between the hydroxyl group of menthol and amino acids. In our future work, research work is being carried out on the determination of the structure of new compounds obtained by YAMR and X-ray structure analysis methods, as well as on the determination of biological activity.

Abbreviations

MS	Mass Spectrometry
IR	Infrared Spectroscopy
HPLC	High Performance Liquid Chromatography

Conflicts of Interest

The authors declare no conflicts of interest.

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