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Origanum cordifolium* **in cover picture was illustrated by Gülten Yeğenağa

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MESSAGE FROM EDITOR IN CHIEF

Dear Colleagues,

We are at the end of 2024. I would like to wish you a happy new year!

As editorial board of EMU Journal of Pharmaceutical Sciences, we also have the pleasure to introduce you the final (3rd) issue of Volume 7, 2024.

Within the content of this issue, there are again quite interesting articles waiting for you to be explored. Physics and pharmacy appear to be different scientific areas. In the review part, the employment of physics in selected pharmaceutical areas has been discussed. The biological evaluation of *Corchorus olitorius* L. (Molokhia) leaves, and folk medicine/morphological characteristics of *Eucalyptus gomphocephala* and *Eucalyptus camaldulensis* in Northern Cyprus have been stated in other research articles. The preparation and evaluation of water-soluble curcumin-cyclodextrin-PVP inclusion complexes generated interesting work. Finally, microwave-assisted synthesis and anticancer activity study for a spiro compound have also been introduced to readers. We are grateful to all authors of this issue.

In the soon period, we are looking forward to your scientific contributions that will be published in EMU Journal of Pharmaceutical Sciences Volume 8 issues of 2025.

Best wishes,

Prof. Dr. H. Ozan Gülcan

Dean of Faculty of Pharmacy
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GUIDE FOR AUTHORS

EMU Journal of Pharmaceutical Sciences (EMUJPharmSci) covers the research on all aspects of Pharmacy presented as original articles, short reports and reviews.

EMU Journal of Pharmaceutical Sciences is published three times (March, August, December) in a year. It is an open access and peer-reviewed journal.

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Reviews: They are limited to 20 pages in addition to supplementary materials (schemes, tables, figures, etc.).

- The original manuscript must be arranged as follows: Title page (including the title, authors and correspondence address), abstract, key words, introduction, materials and methods, results and discussion, acknowledgements and references.
- The reviews must be arranged as follows: Title page (including the title, authors and correspondence address), abstract, introduction, discussion, acknowledgements and references.

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1. General Format

a) All manuscripts can only be submitted electronically via DergiPark.
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c) Use 2.5 cm margins, Times New Roman and format for A4 paper.
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2. Before main text

A. Title page

a) The first page of the manuscript is a title page containing the following information:
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f) Ethical approval should be attached for manuscripts involving studies with human/laboratory animal participants.

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a) The abstract appears on its own page.
b) The abstract should be written in Times New Roman and font size 11.
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e) 3- 6 key words must be provided in alphabetical order (Font: Times New Roman Font Size: 10). Separate the keywords with colon.

3. Main text

A. Introduction

(Font: Times New Roman Font Size: 12)
State the objectives of the work and provide a brief background of the literature related with the topic. The novelty and the aim of the study should be clearly stated.

B. Materials and Methods

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a) Give a brief and clear description of the materials and methods used. Subtitles can be given as appropriate.
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A combined Results and Discussion section is often appropriate. Results should be concise.

Discussion should explore the significance of the results of the work.

Discussion should not repeat the results.

The main conclusions of the study should be presented.

D. Acknowledgement

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Supporting institutions or individuals should be briefly acknowledged just before the reference list.

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- Please ensure that every reference cited in the text is also present in the reference list (and vice versa).
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Examples:

(Sahin, 2000) – one author

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Reference to a journal publication:

Ozhatay N, Kultur S, Gurdal B (2017). Check-list of additional taxa to the supplement flora of Turkey VIII. *Istanbul J Pharm* **47**(1): 31-46.

Ozhatay N, Kultur S, Gurdal B, Ilktac M, Ogmen S, et al. (2019). Check-list of additional taxa to the supplement flora of Turkey X. *Istanbul J Pharm* **57**(2): 35-46.

Reference to a book:

Strunk W Jr, White EB (1979). The Elements of Style. 3rd ed. New York, NY: Macmillan.

Reference to a chapter in an edited book:

Bonati A (1988). Industry and conservation of medicinal plants. In Akerele O, Heywood V, Synge H (eds). The Conservation Medicinal Plants p.141-148 Cambridge University Press UK.

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- Descriptive titles should be given at the top of the tables and at the bottom of the figures.
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CONTENTS

Research articles

Reviews

Research Article EMUJPharmSci ISSN 2651-3587 https://dergipark.org.tr/emujpharmsci

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Synthesis and Anti-Cancer Activity of New Spiro[5.5]undecane Compound by Efficient Microwave Reaction

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Eastern Mediterranean University, Faculty of Pharmacy, Famagusta, North Cyprus via Mersin 10, Turkiye.

Abstract

Microwave-assisted organic synthesis has gained significant attention for speeding up reactions, improving yields, and reducing reaction times. In this study, we investigated the microwave-induced reaction between dimedone and (1E,4E)-1,5-bis(4-fluorophenyl)penta-1,4-dien-3-one to synthesize 7,11-bis(4-fluorophenyl)-3,3-dimethylspiro[5.5]undecane-1,5,9-trione. The reaction was conducted using a microwave irradiation system, which allowed for a more environmentally friendly and energy-efficient process. Key parameters such as reaction time, temperature, and power settings were optimized for maximum yield. The synthesized compound was characterized using spectroscopic methods, including IR, ^{1}H-NMR, ^{13}C-NMR, and mass spectrometry. The same reaction was also performed using a conventional method at room temperature which took 2-3 hours. The microwave approach was preferred due to its efficiency. Our findings indicate that microwave irradiation significantly enhances reaction efficiency, offering a fast method for synthesizing complex organic molecules. This technique has potential applications in various fields, including pharmaceutical chemistry and materials science, with a growing demand for sustainable and efficient chemical processes. Additionally, we conducted an in vitro anti-cancer activity experiment to evaluate the synthesized compound's biological activity.

Keywords

Anti-cancer, dimedone, microwave, synthesis.

Article History

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Article Info

***Corresponding author:** E. Vildan BURGAZ **email:** vildan.burgaz@emu.edu.tr

Research Article:

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DOI: 10.54994/emujpharmsci.1591288

INTRODUCTION

The Spiro[5.5] undecane structure is known to occur in phytochemicals, as well as in alkaloids, terpenoids, and other natural products (Ahmed et al., 2012). Numerous spiro-oxindole derivatives have been found to have a wide range of biological applications, including antimicrobial and antitumor activities, as well as acting as inhibitors of the human NK-1 receptor (Okita and Isobe, 1994; Puri S et al., 2023) Spiro heterocycles and their derivatives were synthesized using dimedone, and the resulting compounds were tested in vitro for their antibacterial activity against Gram negative bacteria including *Escherichia coli* and Gram positive bacteria such as *Staphylococcus aureus* (Majumdar et al., 2018)

Microwave irradiation has various advantages over classical reactions, including greater yields, faster reaction times, and fewer byproducts (Soni et al., 2020). This study focused on developing microwave-assisted synthesis methods for 7,11-bis(4-fluorophenyl)-3,3-dimethylspiro[5.5]undecane-1,5,9-trione **(2a)** through a cascade cyclization process involving a [5+1] double Michael addition reaction.

A literature review reveals limited research on the reactivity of α,β-unsaturated carbonyl compounds with dimedone (**1a**) and there was limited information on the biological activities of the products of the combination of dimedone (**1a)** with the (1E,4E)-1,5-Bis(4-fluorophenyl)penta-1,4-dien-3-one (Ahmed et al., 2011) . Accordingly, we herein report the synthesis of 7,11-bis(4-fluorophenyl)-3,3-dimethylspiro[5.5]undecane-1,5,9-trione (**2a**) from dimedone and (1E,4E)-1,5-Bis(4-fluorophenyl)penta-1,4-dien-3-one (**1b**), along with an investigation of its anticancer activity (Figure 1).

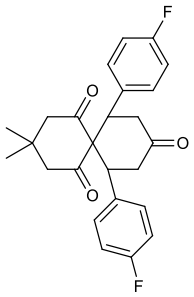

Figure 1: Structural formula of 7,11-bis(4-fluorophenyl)-3,3-dimethylspiro[5.5]undecane-1,5,9-trione (**2a**).

MATERIALS AND METHODS

Chemical and Reagents

Dimedone **(1a)**, p-fluoroaldehyde, dichloromethane, and triethylamine were obtained from Sigma-Aldrich and Merck. Analytical grade chemicals were utilized unless otherwise specified. (1E,4E)-1,5-bis(4-fluorophenyl)penta-1,4-dien-3-one **(1b)** was synthesized through an aldol condensation reaction involving substituted benzaldehydes and acetone in a 2:1 ratio, using an ethanolic NaOH solution as the catalyst as described in our previous research (Burgaz et al., 2024) (Figure 2).

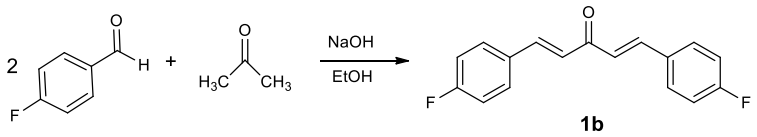

Figure 2: The general synthesis reaction of penta-1,4-diene-3-one derivatives.

^{1}H and ^{13}C NMR spectra were recorded using $CDCl_3$ as the solvent and TMS as the internal reference on a Bruker Avance 400 MHz Spectrometer, as shown in the supplementary information. MS spectra were collected with an Agilent 19091 N-136 GC–MS instrument. A CEM-Focused Microwave™ Synthesis System, which has programmable settings, infrared temperature monitoring, and a continuous microwave power supply system with a tunable output from 0 to 300 W (±30 W), was utilized to conduct microwave-irradiated processes.

Our study aimed to develop microwave-assisted synthesis procedures for 7,11-bis(4-fluorophenyl)-3,3-dimethylspiro[5.5]undecane-1,5,9-trione **(2a)** via a cascade cyclization process involving the [5+1] double Michael addition reaction. The MW-process not only produces high-quality results, but also shortens reaction times from 2-3 hours to about 15-20 minutes. This reaction requires the coupling of dimedone **(1a)** and (1E,4E)-1,5-Bis(4-fluorophenyl)penta-1,4-dien-3-one (**1b)** catalyzed by triethylamine at microwave. This method developed demonstrates exceptional efficiency in producing spiro[5.5]undecane derivative **2a**, achieving yields of up to 98 % (Figure 3).

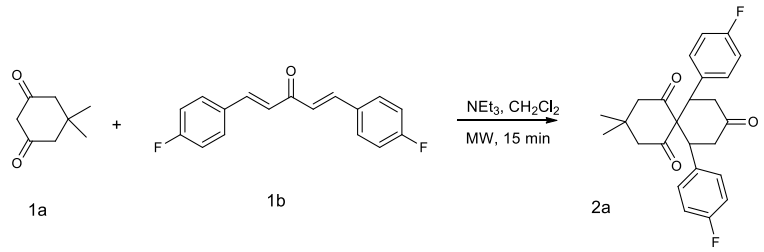

Figure 3: Synthesis reaction of 7,11-bis(4-fluorophenyl)-3,3-dimethylspiro[5.5]undecane-1,5,9-trione (**2a**) from starting materials.

General microwave technique for the synthesis of 7,11-bis(4-fluorophenyl)-3,3-dimethylspiro[5.5]undecane-1,5,9-trione (2a): A mixture of dimedone **(1a)** (1 mmol) and (1E,4E)-1,5-Bis(4-fluorophenyl)penta-1,4-dien-3-one (**1b)** (1 mmol) were weighed into a microwave flask 5 mL CH_2Cl_2 and triethylamine (1.25 mmol, 0.128 g) were added. The reaction mixture was heated under microwave irradiation (200 W, 40 °C) for 15 minutes. The reaction steps are followed by TLC testing. The reaction mixture was put into 10 mL of cold water and extracted using chloroform (3x20 mL). The organic extracts were dried with $MgSO_4$. Column chromatography (gradient, from Hexane: Ethyl Acetate (4/1) was used after solvent evaporation.

Cell culture and cytotoxicity assay

The anti-cancer activity of compound 2a was evaluated against the SK-HEP-1 adenocarcinoma cell line. The cells were kept in DMEM supplemented with 10% FBS, 100 U/mL penicillin, 2 mM L-glutamine, 100 mg/mL streptomycin, and NEAA at 37 °C in humidified CO2 (5%) (ESCO CelCulture® CO_2 incubator) SK-HEP-1 cancer cell lines were subjected to a 48-hour. 3-(4,5-Dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide (MTT) assay to evaluate the anti-cancer activity of the newly synthesized compound. At a density of $5x10^3$ cells/ml, cells were seeded into 48-well plates and subjected to varying doses of the chemicals dissolved in the maintenance medium. DMSO was used as the solvent-control group. The effect of DMSO at peak chemical concentrations was determined to be nonsignificant, the final concentration of DMSO was consistently kept below 1%. Following the 48-hour treatment, the MTT assay proceeded as previously described (Kunter et al., 2023). MTT assays have been carried out three times independently.

RESULTS AND DISCUSSION

The synthesis of new substituted Spiro[5.5]undecane-1,5,9-trione (or 1,3,5,9-tetraone) derivatives has garnered significant interest in recent years because of their possible uses in medicinal chemistry and materials science. In this study, we successfully synthesized 7,11-bis(4-fluorophenyl)-3,3-dimethylspiro[5.5]undecane-1,5,9-trione and characterized it using ^{1}H and ^{13}C NMR spectroscopy, as well as mass spectrometry (MS). Despite numerous proposals in the literature, no consensus has been reached regarding the optimal treatment strategy for hepatocellular carcinoma (HCC), which remains a significant clinical challenge. Although cytotoxic chemotherapeutics are available for clinical use, their efficacy has been limited. Currently, liver transplantation or surgical resection remains the most effective treatment option for HCC. Therefore, there is a pressing need for novel insights to enhance our understanding of HCC and to develop more effective therapeutic strategies. Each newly synthesized compound represents a potential opportunity for advancing therapeutic applications in this context. This study evaluates the anticancer properties of a newly synthesized compound. MTT assay results revealed a statistically significant, concentration-dependent reduction in the viability of the adenocarcinoma cell line SK-HEP-1 (Figure 4). Notably, compound 2a exhibited potent anticancer activity against SK-HEP-1 cells, with an IC_{50} value of 23.67 ± 4 µM.

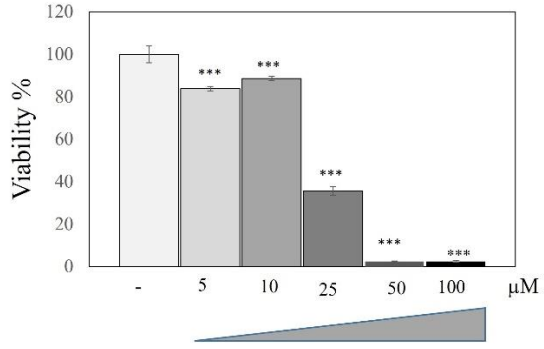

Figure 4: Effect of 2a on the viability of SK-Hep1 cells (MTT). (***p< 0,001).

This synthesized compound exhibits interesting pharmacological activity regarding anti-cancer effect on liver tissue and has shown promise as a building block for designing novel drug candidates.

7,11-bis(4-fluorophenyl)-3,3-dimethylspiro[5.5]undecane-1,5,9-trione (2a)

White solid, (422 mg, 92%). Mp 182-192 ^{0}C. ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.06-7.02 (m, 4H, Ar-H), 6.98-6.94 (m, 4H, Ar-H); 3.80-3.75 (dd, 2H, *J*= 14.4, 4.0 Hz, H_{8e} and H_{10e}); 3.60-3.53 (t, 2H, *J*= 14.4 Hz, H_7); 2.51-2.47 (dd, 2H, *J*= 14.8, 4.0 Hz, H_{8a} and H_{10a}); 2.01 (s, 2H, H_{2a} and H_{4a}), 1.64 (s, 2H, H_{2e} and H_{4e}), 0.14 (s, 6H, CH_3); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 208.28 (C=O), 203.15, 158.78, 156.32, 129.90, 126.10, 111.16, 110.94, 65.02, 51.62, 49.62, 45.34, 39.26, 24.31. MS: 410.17 (411 [M+1]. Anal. calc. for $C_{25}H_{24}F_2O_3$ (410.17): C 73.16, H 5.89, F 9.26; found: C 73.22, H 5.92, F 9.17.

CONCLUSION

In summary, synthesizing the 7,11-bis(4-fluorophenyl)-3,3-dimethylspiro[5.5]undecane-1,5,9-trione (2a) marks a valuable step forward in the quest for new bioactive compounds, particularly within anticancer drug research. Through a microwave-assisted method, we effectively condensed dimedone and (1E,4E)-1,5-Bis(4-fluorophenyl)penta-1,4-dien-3-one, producing a novel compound with notable biological potential. The compound's in vitro anticancer assessments indicate its promising therapeutic prospects, suggesting that further structural modifications in this compound could enhance efficacy and selectivity against cancer cells. This research expands the current synthesis knowledge of spiro[5.5]undecane-1,5,9-trione derivatives and underscores their emerging utility as frameworks for anticancer agents. By positioning our findings within the broader literature, we underscore the critical need for ongoing studies on these derivatives. We aim to inspire new approaches for designing anticancer compounds with enhanced biological properties.

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Kunter I, Zabib N, Goger F, Kosar M (2023). New data for endemic Phlomis brevibracteata Turrill from North Cyprus: biological activities and chemical composition. *Turk J Biochem* **48**: 475.

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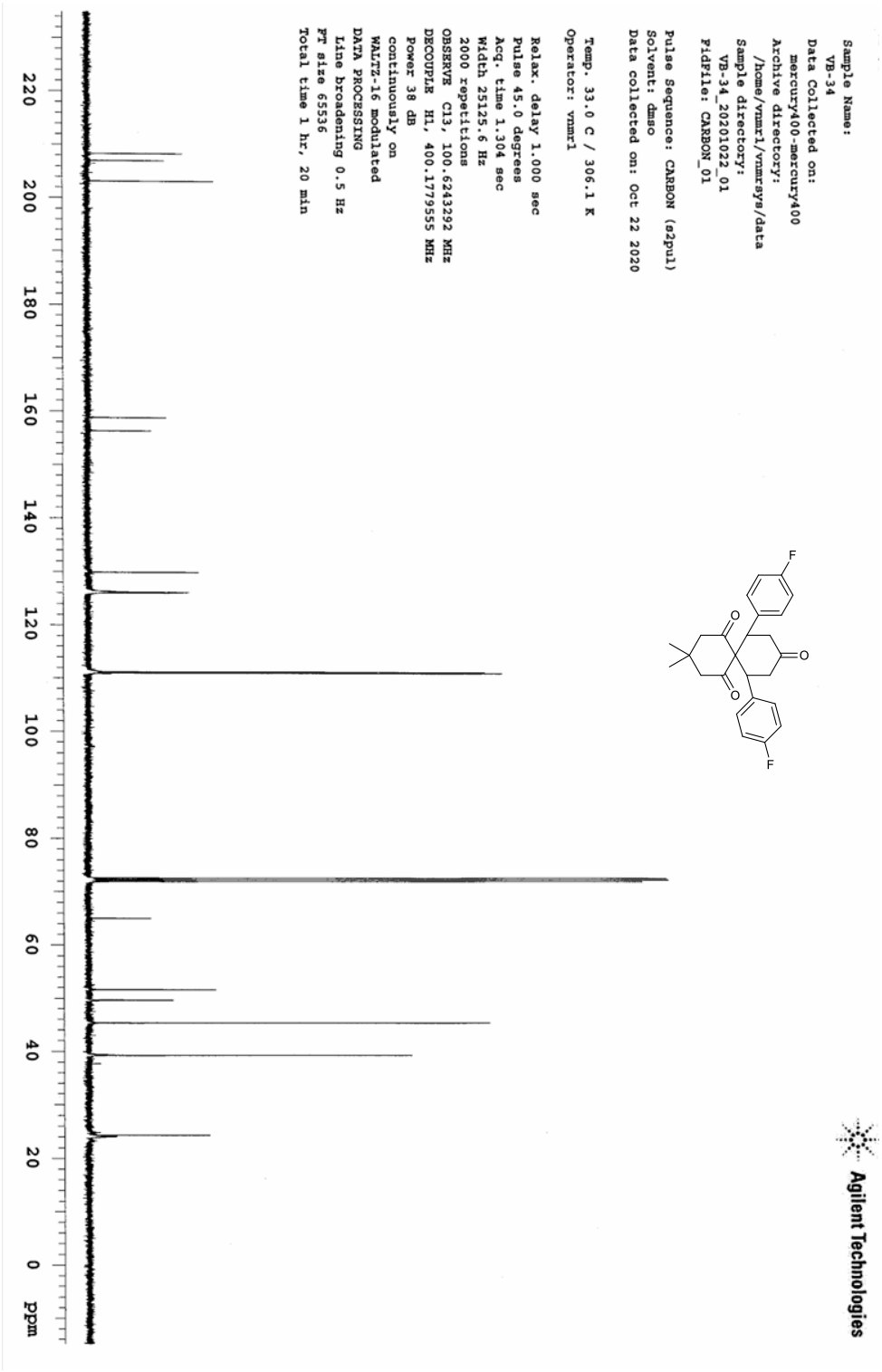
Soni JP, Chemitikanti KS, Joshi SV, Shankaraiah N (2020). The microwave-assisted syntheses and applications of non-fused single-nitrogen-containing heterocycles. *Org Biomol Chem* **18**: 9737.

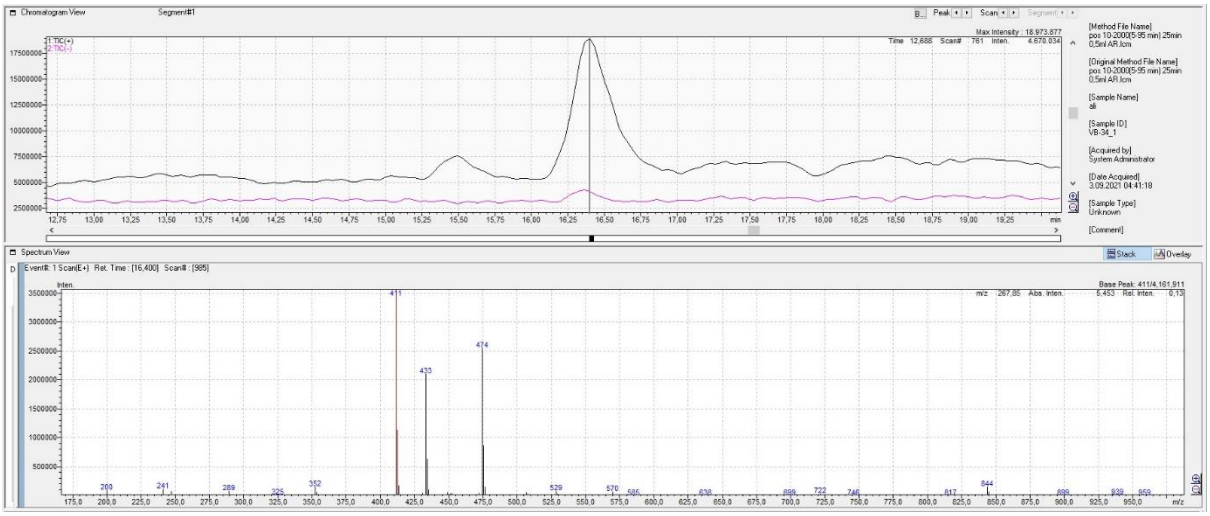
SUPPLEMENTARY INFORMATION

1. ^{1}H-NMR spectrum of **2a** compound.

2. ^{13}C-NMR spectrum of **2a** compound.



3. MS spectrum of **2a** compound.



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Microscopic Evaluation and Qualitative Phytochemical Screening of *Corchorus olitorius* L. (Molokhia) Leaves

Beste Atli*, Nesrin Oztinen, Ezgi Ak-Sakalli, Betul Topalkara, Muberra Kosar

Eastern Mediterranean University, Faculty of Pharmacy, Famagusta, North Cyprus via Mersin 10, Turkiye.

Abstract

Corchrous is a genus which belongs to Tiliaceae family distributed across Asia and Africa. In the world, the *Corchorus* genus encompasses 75 taxa. Widely distributed across the tropics, *Corchorus olitorius* L. (Molokhia) is most likely found in every tropical African nation. Its use as a wild or farmed vegetable has been reported by numerous countries in tropical Africa. In Cyprus, this plant is used to prepare a dish after drying in the summer. The aim of this study was to investigate microscopic evaluation and phytochemical profile of the leaf extracts of *C. olitorius*. In microscopic evaluation experiments, powdered leaf part of the plant was examined under the microscope. For determination of phytochemical profile, some of secondary metabolites were determined qualitatively by chemical reactions. Microscopic analysis revealed that molokhia leaves displayed epidermis, stoma, calcium oxalate crystals, spongy parenchyma, glandular hair, trichome, midrib. The phytochemical profile identification of the leaf extracts of *C. olitorius*, revealed the presence of some active ingredients such as carbohydrates, cardioactives, and flavonoids.

Keywords

Corchorus olitorius, leaf, microscopy, plant tissue, phytochemistry.

Article History

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DOI: 10.54994/emujpharmsci.1595726

INTRODUCTION

Corchorus olitorius L., also known as molokhia, Egyptian spinach, Nalta jute, or Tossa jute, is a member of the Tiliacea family (Table 1). The annual plant *C. olitorius* that can reach a height up to 2-4 meters and is stiff and fibrous (Islam, 2013). Its border leaves are sharply indented and alternate. *C. olitorius* produces tiny yellow blooms with five petals that eventually develop into a brown, multiseeded pod (Loumerem et al., 2016). It is spread by seeds and can be grown in household gardens or tolerated as a wild vegetable in crop fields (Begum et al., 2011).

Table 1: Taxonomy of *C. olitorius* L. (Islam, 2013).

Rank	Scientific Name and Common Name
Kingdom	Plantae – Plants
Subkingdom	Tracheobionta – Vascular plants
Superdivision	Spermatophyta – Seed plants
Division	Magnoliophyta – Flowering plants
Class	Magnoliopsida – Dicotyledons
Subclass	Dilleniidae
Order	Malvales
Family	Tiliaceae – Linden family
Genus	*Corchorus* L. – corchorus
Species	*Corchorus olitorius* L. – nalta jute
	Corchorus capsularis L. – white jute

This dark green leafy vegetable is widely consumed as food in the Middle East, Eastern Mediterranean, and Cyprus. Young leaves are tasty and soft, however older leaves become woody and fibrous, rendering them less suitable for consumption (Soykut et al., 2018). Known as a popular leafy soup, it is prevalent in all tropical and sub-tropical climates (Kundu et al., 2012). It is considered a nutrient-dense vegetable because of its high concentration of vitamins and other nutraceutics such as vitamin B1, B2, A, C, E, folic acid, minerals, *beta*-carotene, calcium, and iron. High levels of phenolic components, such as quercetin and caffeoylquinic acids, suggest that it may possess antioxidant qualities and be linked to protection against chronic illnesses such as diabetes, cancer, heart disease, and hypertension (Giro et al., 2016). *C. olitorius* is used to treat ulcers, heart failure, female infertility, typhoid fever, and malaria in West Africa (Nyadanu et al., 2017). In addition to its antidiabetic actions (Airaodion et al., 2019), the vegetable was reported to possess antibacterial (Ilhan et al., 2007), anti-inflammatory (Handoussa et al., 2013), antiobesity (Wang et al., 2011), and gastroprotective qualities (Nakaziba et al., 2020). Seeds of *C. olitorius*, have been used as demulcents, diuretics, and purgatives, as well as in cases of chronic cystitis. The seeds can also be used against heart failure because they contain cardenolides, also known as cardiac glycosides (Al-Yousef et al., 2017). The leaves have been used to treat tumors, colds, fevers, constipation, gonorrhea, and chronic cystitis (Islam, 2013, Zakaria et al., 2006). Although other parts can also be used the

leaf is the most frequently used part of the plant in folk medicine. The parts used in traditional medicine and the areas of use of these parts are given in Table 2.

Table 2: Usage of *C. olitorius* L. in traditional medicine (Adebo et al., 2018).

Usages	Parts of the plant used
Malaria	Whole plants, leaves, roots, leafy stems
Typhoid fever	Leafy stems, flowers, roots, leaves, whole plant
Fever	Leafy stems, flowers, leaves, whole plant
Female fertility	Whole plant
Diarrhea	Leaves
Ulcera, Colic	Leafy stems, leaves, leaves and seeds, whole plant
Itera	Leaves, leafy stems
Heart failure	Whole plant
Child malnutrition	Leaves
Sexual weakness	Roots

C. olitorius contain many different secondary metabolites such as phenolic acids, flavonoids and some steroidal compounds. The leaves and the flower parts of the plant are rich in hydroxycinnamic acid derivatives such as caffeic, coumaric, rosmarinic and ferulic acid. Flavonoid derivatives (luteolin, apigenin, quercetin, kaempferol, rutin, and naringenin) were identified in leaves and flowers. In addition, steroidal compounds such as stigmasterol, β-sitosterol, canarigenin, fusudic acid, and campestrol were detected in the seed of the plant (Abdel-Razek et al., 2022).

MATERIALS AND METHODS

The dried leaves of *C. olitorius* L. were purchased from a market in Famagusta, Cyprus in September 2024. The plant was identified using Flora of Cyprus (Meikle, 1977). Microscopic materials and chemical reagents were supplied from Eastern Mediterranean University Laboratories.

Microscopic evaluation of *C. olitorius* L. leaves

For the microscopic studies, leaf sample was fine powdered and mounted in chloralhydrate reagent. Microscope slide was heated with Bunsen burner for fixation of the sample and the microscopical characteristics of leaf powder were investigated.

Phytochemical screening of *C. olitorius* L. leaves

Test for carbohydrates

After 7 gr of the plant sample was weighed and crushed using mortar and pestle, it was transferred to the beaker. 40 mL of distilled water was added to the crushed plant sample in the beaker and stirred for 5 minutes. The aqueous part of the suspension is filtered off. 3.5 mL of 10% lead acetate solution was added to the filtrate drop by drop followed by filtration of the solution. Through this process, compounds such as chlorophyll, flavonoids, and tannins are

precipitated and separated from the aqueous extracts. 4 mL of 2.5% disodium hydrogen phosphate was added dropwise to the filtrate, and then the solution was filtered. Extract was used for the determination tests.

Fehling test: 1 mL of the extract prepared as mentioned above is replaced in a test tube. 2 mL of Fehling A and then 2 mL of Fehling B were added to the extract. The solution was heated using bunsen burner. Formation of red colored Cu_2O shows precipitation that indicates the presence of a carbohydrates.

Molisch test: To 1 mL of the extract, 5 drops of 5% alcoholic α-naphthol solution was added in a test tube. The test tube was slightly tilted and concentrated sulphuric acid was leaked down into the tube, where formation of violet-purple ring proves the presence of a carbohydrate.

Seliwanoff test: 2.5 mL of Seliwanoff reagent was added to 1 mL of the extract in a test tube. Then, the solution was subjected to boil. Formation of red color indicates the presence of a ketose in the solution. Aldoses give late reaction results, and their presence produces light red color. On the other hand, saccharides such as pentoses lead the formation blue-green color.

Test for flavonoids

2% decoction was prepared from the powdered plant sample that is dissolved in 15 mL of 50% ethanol solution.

Ferric chloride test: 2-3 drops of 5% $FeCl_3$ solution in water were added to 3 mL of the extract. Green and blue-black colour indicates the presence of flavonoids.

Sodium hydroxide test: 2-3 drops of 10% NaOH solution were added to 3 mL of the extract. Bright yellow color indicates the presence of flavonoids.

Sulphuric acid test: 2-3 drops of sulphuric acid solution were added to 3 mL of the extract. Red color formation indicates the presence of flavonoids.

Cyanidin (Shinoda-Shibata) test: 0.5 mL of concentrated hydrochloric acid and magnesium or zinc dust at the tip of spatula were added to the filtrate, where hydrogen gas release is observed by bubbles causing an orange color for flavones, a red color for flavonols, and a purple color for flavanones.

Test for cardioactive glycosides

1 gr of the powdered plant sample was boiled for 3 minutes with 25 mL of 50% ethanol in a water bath and then filtered off. Into the filtrate, 5 mL of 10% lead acetate was added where precipitation was observed. Precipitation was filtered off and the filtrate was hydrolysed by heating with diluted sulphuric acid for 3 minutes. 1 mL of the solution was taken into a test tube for Keller-Kiliani reaction and the rest was mixed with chloroform in a separating funnel. The organic chloroform layer (bottom layer) was taken and used in Baljet test.

Baljet's test: 5 mL of the dissolved extract was evaporated in a capsule. 1 mL of Baljet reagent and 5 drops of 6% sodium hydroxide were added to the test tube. Formation of an orange color displays the presence of a cardenolides.

Keller-Kiliani reaction: To a small amount of solution separated in a test tube, sulfuric acid was leaked from edge of the tube, where two layers were formed. Formation of a brown-red ring between the two layers shows the presence of 2-deoxy sugars.

Test for saponins

Foam test: 0.5 gr of the powdered plant was placed in a test tube with 10 mL hot water. After cooled down, it was shaken vigorously for approximately 10 seconds. In the presence of saponin, a foam layer of 1-10 cm in height forms, which remains stable for at least 10 minutes and does not disappear with the addition of 1-2 drops of 2 N HCl.

RESULTS

Microscopic evaluation of *C. olitorius* leaves

Powdered leaf sample was mounted in chloral hydrate reagent. After investigation under microscope; epidermis, stoma, calcium oxalate crystals, spongy parenchyma, glandular hair, trichome, and midrib elements were detected (Figure 1).

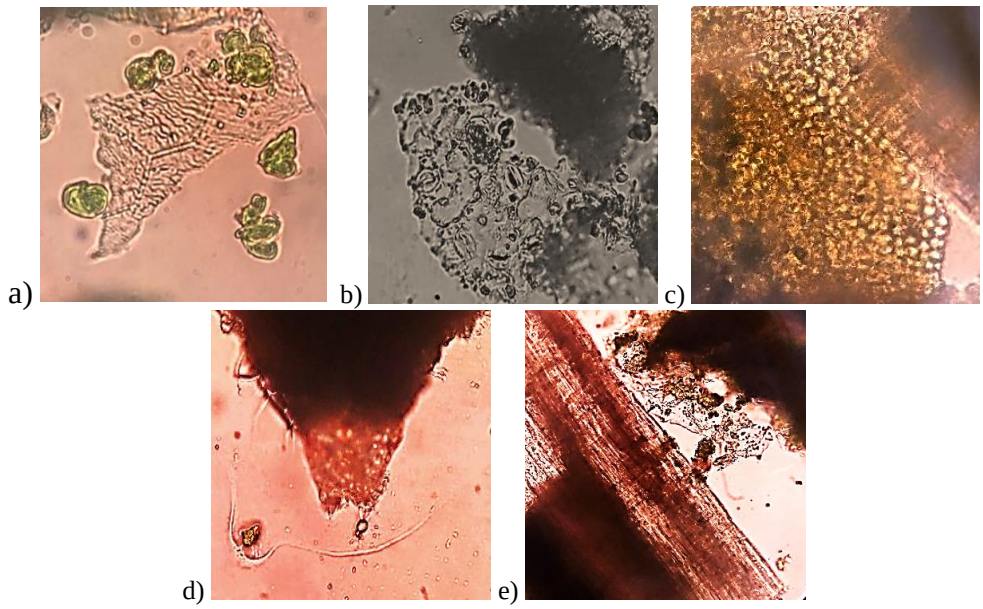

Figure 1: Microscopic images of *C. olitorius* leaves.
a: epidermis, b: stoma and calcium oxalate crystals, c: spongy parenchyma, d: glandular hair and trichome, e: midrib.

Phytochemical screening of *C. olitorius* L. leaves

In the present study, phytochemical screening was crucial for discovering novel sources of chemicals with therapeutic and industrial use that have been chemically studied in medicinal

plants. Primary and secondary metabolites were qualitatively analysed. The phytochemical profile revealed the presence of some active ingredients such as carbohydrates, cardioactive glycosides, and flavonoids (Table 3).

Table 3: Qualitative phytochemical screening of *C. olitorius* leaves.

Primary/Secondary metabolites	Results	Name of tests
Carbohydrates	+	Fehling test, molisch test, seliwanoff test
Flavonoids	+	Ferric chloride test, sodium hydroxide test, sulphuric acid test
Cardioactive glycosides	+	Baljet's test, Keller-Kiliani test
Saponins	-	Foam test

DISCUSSION

In a previous study, microscopic evaluation of *C. olitorius* showed the presence of epidermis, stomata, glandular hair, and trichome (Varban et al., 2021). In another study, the surface view, transverse section and the powder of *C. olitorius* leaves were analysed under microscope and the presence of midrib non-glandular trichomes, epidermis, palisade parenchyma, spongy parenchyma, stoma and phloem were observed (Khan et al., 2022). As a results of the examination of the leaf of *C. capsularis* under the microscope, the presence of epidermis, stomata, calcium oxalate crystals, spongy parenchyma, trichome, and midrib similar to *C. olitorius* except glandular hair was detected (Mallesh et al., 2023).

Phytochemical characteristics of *C. olitorius* were investigated by numerous studies. In one of the studies, it was found that fresh *C. olitorius* leaves consisted of steroids, cholesterol, alkaloids, phenols, flavonoids, riboflavin, saponins, and terpenoids (Sadat et al., 2017). The ethanolic extract of dried *C. olitorius* leaf revealed the presence of tannins, steroids, saponin, terpenoids, cardiac glycosides, and alkaloids as chemical constituents (Ujah et al., 2014). Although microscopic and phytochemical studies conducted on this species are present, studies conducted on the species grown in Cyprus are limited.

Microscopic evaluation and phytochemical analysis are very important to identify plant species. Further studies are needed to characterize *C. olitorius* species in detail.

CONCLUSION

In conclusion, the present study will provide a background for the characteristics and phytochemistry of *C. olitorius* leaf. Further pharmacognostic analysis of the leaf will offer specific criteria for accurate identification. Phytochemical and instrumental analyses alongside biological activity studies related to the plant's traditional uses are among future directions.

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Assessment of the Usage in Folk Medicine and Morphological Characteristics of *Eucalyptus gomphocephala* and *Eucalyptus camaldulensis* in Northern Cyprus

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Abstract

One of the most significant and extensively planted genera in the world is *Eucalyptus*, which consists of tall, evergreen trees with leathery leaves. They are indigenous to Australia and comprise more than 900 species and subspecies. About 62 species of *Eucalyptus* may be found in Cyprus; 47 of these are named, while the remaining 15 are hybrid or unclassified. Traditional medicine uses a variety of *Eucalyptus* species as an antiseptic and to treat upper respiratory tract illnesses. By inhaling the essential oil extracted from these plants, pulmonary infections can be treated therapeutically. The purpose of this study was to provide information on the physical characteristics of *Eucalyptus gomphocephala* DC. and *Eucalyptus camaldulensis* Dehnh., as well as to investigate the traditional usage of *Eucalyptus* trees in North Cyprus.

It has been noted that there are numerous differences between the two species' flower buds, flowers, fruits, and barks. This study, conducted in Northern Cyprus, is to record and inform Eastern Mediterranean University Faculty of Pharmacy students and staff on the traditional uses of *Eucalyptus* species by various nations (Turkiye, Cyprus, Iran, Nigeria, Uganda).

One hundred informants whose ages ranging from 20 to 60 were interviewed in person for the study. Questions concerning the use of *Eucalyptus* plants, where they come from, which parts of the plant are used, and how they are used were asked to interviewees, who ranged in age from 20 to 60.

Observations have led to the widespread use of *Eucalyptus* by Iranian and Turkish Cypriots, Boiling the leaves and using the steam to enhance respiratory health was the most frequently used method in the local application of the plant in the treatment.

Keywords

Eucalyptus camaldulensis, *Eucalyptus gomphocephala*, folk medicine, North Cyprus

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INTRODUCTION

Eucalyptus gomphocephala DC. and *Eucalyptus camaldulensis* Dehnh. belong to the Myrataceae family. Myrtaceae include about 5,950 species in about 132 genera. *Eucalyptus* is a genus of flowering plants with more than 700 species from the Myrtaceae family. *Eucalyptus* is a cultivated tree originated in Australia. All species of the family are evergreen trees and rich in organic hydrosols (Bachir and Benali, 2012; Adediran, 2021; Adediran et al., 2021; Tsintides et al., 2002).

French agriculturist Madon was the first to bring *Eucalyptus* to Cyprus. Madon, in 1876, was sent to Cyprus by the Ottoman administration to prepare a report regarding existing forests (Yıkıcı, 2015). *Eucalyptus* trees dry up swamps and prevent malaria. During XVII. and XIX. centuries, *Eucalyptus* trees were used to drain swamps that were the source of malaria in Cyprus (Gorcelioglu, 1988).

Eucalyptus trees are widely used for health-improving purposes to fight against malaria. They also play a vital role in producing pollen for bees by flowering during the long, dry periods of the year. The trees can grow on chalky and clayish hills. *E. gomphocephala* DC. (tuart) and *E. camaldulensis* Dehnh. (river red gum) are flowering in late summer, especially from October to December during which honey bees can feed on the plants.

E. gomphocephala is a tree up to 40 meters tall. *E. gomphocephala* leaves are green lanceolate in shape, petiolate leaf with alternate leaf position, base attenuate, and the tip is mucronulate. Stem is smooth orange with orange petiole and pith glands of the stem are absent. The flower is a creamy in colour. Fruit with campanulate shape and orange colour has a shiny wax and slight fruit ribbing.

E. camaldulensis is an evergreen tree up to 30 meters high with whitish, yellowish or greyish patches after irregularly decorticated bark; simple, leathery leaves which are aromatic when crushed; glaucous green young leaves and dull green or pallid green mature leaves. Flowers are 5-10 in axillary umbels and appear from March to May. Fruits that re woody capsules ripen from August to September. It is an exotic tree in Cyprus and widely cultivated in the lowlands (Tsintides et al., 2002). *E. camaldulensis* (commonly known as the river red gum) typically grows on river edges and live up to a thousand year. This tree generally has a single stem, and a large trunk, and can grow as tall as 30-45 meters (Ghasemian et al., 2019). The trunk diameter of this species is usually between 1-2 meters. Leaves are alternate, with grey-

blue color, length is 8-22 cm long, width is 1-2 cm, often curved or sickle-shaped, tapering, short pointed at the base. The inflorescence is auxiliary, solitary, 7-11 flowered; flower buds are white, globularrostrate or ovoid-conical; operculum is hemispherical, rostrate or conical, 4-6 x 3-6 mm, obtuse. The flowering period is between August and November (Ozan, 2011). The bark is smooth and can have colour variations of white, yellow, green, grey, and pink. The barks of *E. camaldulensis* occasionally shred in strips or irregular flakes. Fruits are capsule, small, and contain tiny seeds (Al-snafi, 2017).

Studies about phytochemicals of *Eucalyptus* species are generally related to essential oils (EO) due to its high eucalyptol (1,8-cineole), caryophyllene and carvacrol in its composition. In addition to EOs, it includes many secondary metabolites. These are flavonoids (rutin, hyperin), phenolics, tannins, caffeic acid, and waxes. Phytochemicals and medicinal activities of the *Eucalyptus* tree were investigated by many studies. The EOs of *E. camaldulensis* have spasmolytic and antioxidative activities, and cytotoxic effects (Al-snafi, 2017). Research on antibacterial activity and phytochemicals of water-distilled EOs from leaves of *E. camaldulensis* collected from the North part of Cyprus was conducted. The findings showed that ethanone, eucalyptol (1,8-cineole), caryophyllene, and carvacrol were major components of the EO (Akin et al. 2010). In addition, the antibacterial activity of the vapor of *E. camaldulensis* EO from was investigated in another study. The findings showed that it inhibited the growth of both *Staphylococcus aureus* and *Escherichia coli*. 1,8-cineole was the major component, and terpeniol was the main contributory component for its antibacterial activity that exhibited an eight-fold higher effect than 1,8-cineole against *S. aureus* (Ghalem and Mohamed, 2008). Antimicrobial activity of 1,8-cineole against many bacteria including *Mycobacterium tuberculosis* and methicillin-resistant *Staphylococcus aureus* (MRSA), viruses, and fungi (including *Candida*) was reported (Sadlon Lamson, 2010). Antioxidant and antidiabetic activities of the EO of *E. camaldulensis* were documented in detail for the first time by Basak and Candan (2010). The tree also has analgesic, anti-inflammatory, antioxidant, immune-stimulatory, and spasmolytic activities. Vapor inhalation or oral route can be used in both purulent and non-purulent respiratory problems, including chronic obstructive pulmonary disease (COPD), bronchitis and asthma (Sadlon Lamson, 2010). 1,8-cineole, *p*-cymene, β-pinene, terpinen-4-ol, and globulol are the main chemicals found in EO of *E. camaldulensis* leaves (Pagula et

al., 2000). The species identification, chemical composition, and antibacterial activity of the fruits and leaves of *E. gomphocephala* were examined by Stankov et al. (2020). The fruits and leaves had 0.34% and 0.23% EO in their compositions, respectively. 1,8-cineole (46.69%), *p*-cymene (8.99%), baeckeol (8.57%), α-pinene (5.21%), and globulol (4.25%) were the primary constituents of tuart fruits' EOs whereas 1,8-cineole (24.25%), *p*-cymene (20.70%), α-pinene (14.15%), β-pinene (8.17%), γ-terpinene (6.90%), methyleugenol (6.78%), α-terpineol (4.75%), and limonene (3.80%) were the primary contents of tuart leaves' EOs. Additionally, they discovered that the EO of tuart leaves displayed more pronounced antimicrobial activity than fruit EO against all tested microorganisms (*S. aureus, Bacillus subtilis, Kocuria rhizophila, E. coli, Pseudomonas aeruginosa, Salmonella* Abony, *Saccharomyces cerevisiae, Candida albicans,* and *Aspergillus brasiliensis*) (Adediran, 2021).

A diverse range of biological activities has been reported for many compounds including flavonoids, tannins, phloroglucinol derivatives and terpenoids isolated from different *Eucalyptus* species. Gallic acid, quercetin, myricetin, chlorogenic acid, gentisic acid, and ellagic acid have been reported as components of *E. gomphocephala* and the EO constituents of *E. gomphocephala* included α-pinene, β-pinene, limonene, myrcene, 1,8-cineole, allo-aromadendrene and globulol (Al-Sayed et al., 2010).

Eucalyptus has a traditionally important role in Cyprus. Its leaves are widely used in folk medicine. The method of using *Eucalyptus* is breathing the vapor over a cauldron of boiling water containing the leaves with a towel-tent over the head. Sometimes, orange peel, lemon peel, rosemary, or myrtle are added to *Eucalyptus* leaves. This method is called ‘Thermo’ or ‘Hermo’ by local people. It is widely used against congestion, cough, bronchitis, cold and flu, asthma, sinusitis and for well-being in the postpartum period. Feet are put into the hot water containing *Eucalyptus* leaves against foot pain. Myrtle branches, orange, and lemon peel may be added beside *Eucalyptus* leaves against menstrual pain. The oil obtained from crushed leaves is used externally to relieve pain. The layer of leaves and olive oil are applied onto warts.

Local name of *E. camaldulensis* is Efgalitto or Okaliptus in North Cyprus. Preparation of *E. camaldulensis* for local usage is as follows: 10 leaves are boiled in 3 L water, and the resulting steam is inhaled. The steam obtained by boiling the leaves is used to treat flu, cold, and cough and relieve congestion.

MATERIALS AND METHODS

As plant material, *E. gomphocephala* and *E. camaldulensis* were collected from the Salamis forest at Famagusta region of Northern Cyprus, in October 2024 (Figure 1). The plant samples were identified, and the macroscopic and microscopic characterizations of herbal substances were conducted. Herbarium specimens (voucher numbers TE007 and TE008) were deposited and retained in the herbarium at Eastern Mediterranean University, Faculty of Pharmacy. Information such as local names, areas of use, parts used, preparation methods, and usage dosages of these plants were recorded.

Figure 1: Study area: Salamis forest (Map showing the location of Famagusta, North Cyprus).

a **b** **c** **d**

Figure 2. Flowers' buds (a), Flowers (b), fruits (c) and barks (d) of *E. gomphocephala*.

Flowers buds, Flowers, fruits, and barks of *E. gomphocephala* (Figure 2) and *E. camaldulensis* are shown in Figure 2 and Figure 3.

a **b** **c** **d**

Figure 3: Flowers' buds (a), Flowers (b), fruits (c) and barks (d) of *E. camaldulensis.*

In this study, it was aimed to collect data about the traditional usages of *Eucalyptus* species in different countries (Turkiye, Cyprus, Iran, Nigeria, Uganda) via a questionnaire conducted on 100 students and workers in Eastern Mediterranean University (EMU) Faculty of Pharmacy students and staff. Face-to-face interviews were conducted with students and the staff at EMU Faculty of Pharmacy. The participants were asked whether they have ever used *E. camaldulensis* for any local treatment. The participants who used the plant as a part of local treatment were interviewed about its usage, the part of the plants used and the method of application.

RESULT AND CONCLUSION

Of 100 participants, 50 reported that they have used *E. camaldulensis* as a part of local treatment. The plant's local use distribution by age group and nationality is displayed in Table 1. 27 (69.2%) Turkish Cypriots and 15 Iranians (100%) reported using *E. camaldulensis* as a local remedy. Only 5 (12.5%) out of 40 Turkish participants utilized *Eucalyptus* as a local remedy. Additionally, participants from Iran, Uganda, and Nigeria demonstrate that they use *Eucalyptus* as a local remedy.

Table 1: Distribution of the local use of the plant according to the nationalities and age groups.

	Age Groups (years)										
	20-30		**30-40**		**40-50**		**50-60**		**All**		**Total**
Country	**Y***	**N***	**Y**	**N**	**Y**	**N**	**Y**	**N**	**Y**	**N**	**Total**
Turkiye	5	33	0	0	0	2	0	0	5	35	40
Cyprus	8	12	10	0	2	0	7	0	27	12	39
Nigeria	3	3	0	0	0	0	0	0	3	3	6
Iran	12	0	0	0	0	0	0	0	12	0	12
Uganda	3	0	0	0	0	0	0	0	3	0	3
Total	**31**	**48**	**10**	**0**	**2**	**2**	**7**	**0**	**50**	**50**	**100**

*Y: Yes; N: No

The ages of the participants ranged from 20 to 60 years. In general, 39.2% (n=31) of participants whose ages ranged from 20-30 years used *Eucalyptus* for the treatment. All of 17 participants older than 30 years old responded that they have heard about the

usage of *Eucalyptus* as a local treatment in their countries (Table 1).

The majority of the interviewees stated that they learned the use of this medicinal plant from their parents and older relatives. Some of the participants stated that they inspect the fruits of the tree before collecting the leaves, while the others stated that they ask the elderly relatives which tree they need to gather for their own purpose. The locals, especially those who were older than 30 years old, said they can easily distinguish and utilize *E. camaldulensis* from other *Eucalyptus* species particularly because of its leaf odor. One of the primary differences in identifying *E. gomphocephala* as shown in Figure 2d, is the tree's bark; in Figure 3d, the barks of *E. camaldulensis* are different. The tree's body appears to have been peeled off, and it is light brown in color. The bark of the other species, *E. gomphocephala* (Figure 2d), is darker, and its body is dark brown, almost black. There are apparent differences between the flower buds and fruits of the *E. gomphocephala* (Figure 2a-c) and *E. camaldulensis* (Figure 3a-c) trees.

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Preparation and Evaluation of Water-Soluble Curcumin-Cyclodextrin-PVP Inclusion Complexes

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Abstract

Curcumin, the principal bioactive constituent of turmeric, has attracted considerable interest because of its therapeutic attributes, which encompasses anti-inflammatory, antioxidant, and antimicrobial effects. Nonetheless, its clinical utilization is impeded by inadequate water solubility and diminished bioavailability. This research sought to improve the solubility and antimicrobial efficacy of curcumin by creating inclusion complexes with *β*-cyclodextrin and polyvinylpyrrolidone. Curcumin-*β*-cyclodextrin-polyvinylpyrrolidone complexes were formulated using the kneading method with different polyvinylpyrrolidone concentrations (0.5%, 1%, and 1.5%). Solubility investigations revealed that the 1.5% polyvinylpyrrolidone complex demonstrated a 30-fold increase in solubility relative to pure curcumin. UV-visible spectrophotometry validated the enhancement of solubility, whereas optical microscopy and particle size analyses underscored the uniformity and stability of the complexes. The dissolution profile of the optimized complex demonstrated markedly improved drug release under physiological conditions. Additionally, antimicrobial assays revealed enhanced efficacy of curcumin-curcumin-*β*-cyclodextrin-polyvinylpyrrolidone complexes against Gram-positive bacteria, specifically *Staphylococcus aureus* and *Enterococcus faecalis*. The findings indicate that Curcumin-*β*-cyclodextrin-polyvinylpyrrolidone inclusion complexes present a viable approach to address the solubility and bioavailability issues of curcumin, facilitating its broader use in pharmaceutical formulations.

Keywords

β-Cyclodextrin, curcumin, polyvinylpyrrolidone, solubility enhancement, spectrophotometry.

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INTRODUCTION

Turmeric (*Curcuma longa*), widely known as the "golden spice" or "Indian saffron," has been a cornerstone of traditional medicine and cultural practices for over 4,000 years, originating from the Vedic culture in India. Its therapeutic value lies in curcumin (CUR), the primary bioactive compound responsible for its vibrant yellow color and extensive medicinal applications. CUR has garnered significant scientific interest for its potent anti inflammatory, antioxidant, antibacterial, and anticancer properties, making it a subject of extensive research in contemporary biomedical science (Hewlings and Kalman, 2017).

CUR, a hydrophobic molecule with a log P of 3.2, is practically insoluble in water and has a short half-life of approximately 10 minutes in phosphate buffer at physiological (pH 7.4) due to its instability in alkaline conditions (Hegde et al., 2023).

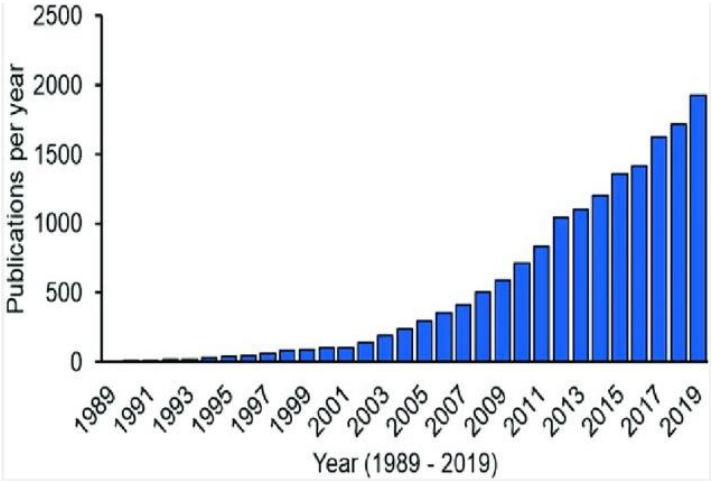


Figure 1: The number of publications indexed by “PubMed” with the topic “curcumin during the last three decades.

As shown in Figure 1, Turmeric and its active component, CUR, have been extensively studied, with nearly 7,000 publications on Turmeric and over 20,000 on CUR indexed in PubMed. (Kunnumakkara et al., 2023).

Turmeric is recognized as a safe food ingredient by the United States Food and Drug Administration (FDA). Turmeric's therapeutic potential has been documented since 1876 when its flower was first reported effective against gonorrhea. Since then, turmeric has been reported for its efficacy against various chronic diseases, including skin conditions, respiratory and gastrointestinal disorders, aches, wounds, sprains, and liver malfunctions. Reports indicate that CUR, along with its

derivatives demethoxycurcumin and bisdemethoxycurcumin, is non-toxic even at high doses of up to 12,000 mg/day. CUR's antibacterial activity was first reported in 1949 when it was shown to inhibit the growth of *Staphylococcus aureus*. Beyond its antimicrobial effects, CUR is recognized for its broad pharmacological benefits, including anti inflammatory, antioxidant, antimutagenic, immunomodulatory, and chemotherapeutic properties. It effectively scavenges reactive oxygen species (ROS), mitigating inflammation and playing a regulatory role in the pathophysiology of chronic diseases by modulating key signaling pathways and enzymes. These attributes underscore CUR's potential as a versatile therapeutic agent for combating infections and chronic disorders (Kunnumakkara et al., 2019; Lao et al., 2006; Schraufstätter and Bernt, 1949).

Despite its potential, CUR's effectiveness is significantly limited due to its poor water solubility, instability in aqueous environments, and rapid breakdown in the body, resulting in low bioavailability (Stohs et al., 2020).

Developing novel strategies to enhance CUR's solubility and stability remains a critical focus for researchers aiming to maximize its therapeutic potential. To achieve this, various formulation approaches can be employed to improve CUR's stability, solubility, and bioavailability. These strategies which are widely used to enhance its physicochemical properties include nanoemulsions, liposomes, and nanoparticles (Figure 2). Additionally, cyclodextrin inclusion complexes, particularly with *β*-cyclodextrin (*β*-CD), are effective encapsulation agents that significantly improve CUR's solubility and stability.

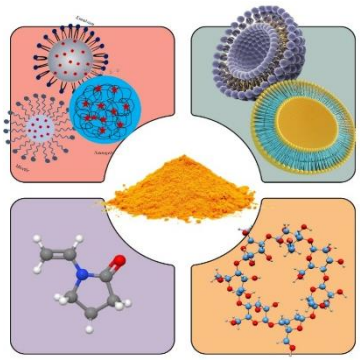


Figure 2: Strategies for increasing curcumins aqueous solubility**.**

Incorporating polyvinylpyrrolidone (PVP) as an excipient further enhances the pharmacokinetic profile of CUR. PVP, a water-soluble polymer, serves as a stabilizing agent by preventing complex precipitation and improving dispersibility

in aqueous environments. This contributes to enhanced formulation stability and improved bioavailability, enabling more efficient absorption of CUR in the body.

Furthermore, the use of cyclodextrins, cyclic oligosaccharides with a well-established ability to enhance the solubility and stability of hydrophobic drugs, is a promising strategy. β-CD, in particular, is known for its ability to form inclusion complexes with poorly soluble molecules, encapsulating them within its hydrophobic cavity while maintaining an outer hydrophilic shell, which improves both stability and solubility. By combining these innovative strategies, CUR can be delivered more effectively, enhancing its therapeutic efficacy (Aiassa et al., 2023; Loftsson and Brewster, 2010b; Sarabia-Vallejo et al., 2023). The synergistic use of β-CD and PVP has shown promise in enhancing the solubility and functional properties of various bioactive compounds.

Even with recent progress, the potential of β-CD and PVP inclusion complexes to boost CUR's solubility and antimicrobial activity has not been fully explored. Previous studies have primarily focused on solubility improvements, with limited emphasis on functional evaluations such as antimicrobial activity (Loftsson and Brewster, 2010a; Schoeman et al., 2024; Stohs et al., 2020). The present study seeks to bridge this gap by not only enhancing CUR's solubility but also evaluating its functional bioactivity including antibacterial assays to assess the functional efficacy against common pathogenic bacteria.

This research stands out for its comprehensive method, merging the solubility-enhancing properties of β-CD and PVP with practical evaluations to showcase the potential of these complexes as cutting-edge drug delivery systems. The primary objective of the study is to develop and characterize CUR-β-CD-PVP inclusion complexes, quantify their impact on solubility, and evaluate their antimicrobial properties. By addressing both the physicochemical and biological aspects of CUR enhancement, the present study aims to contribute to the development of efficient CUR-based formulations, paving the way for broader applications in the pharmaceutical and biomedical fields.

MATERIALS AND METHODS

Materials

Curcumin for synthesis was obtained from Merck (Darmstadt, Germany), methanol was purchased from Merck (Darmstadt, Germany), *β*-Cyclodextrin was obtained from Sigma Aldrich (Saint-Quentin Fallavier, France), PVP K-30 was purchased from Zag Kimya cosmetic grade (Turkiye) and cellulose acetate syringe filters with a pore size of 0.45 µm were from ISOLAB (Eshau, Germany). Studies were conducted using distilled water.

Preparation of curcumin *β*-Cyclodextrin-PVP complex

As shown in Table 1, three formulations were prepared using the kneading method. Precisely weighed quantities of CUR, *β*-CD, and PVP were combined in a mortar. A mixture of water and methanol in a 1:1 ratio was incrementally added to the components, forming a paste. The resulting paste was subjected to drying in an oven maintained at a temperature not exceeding 50°C for a duration of 10 minutes. After drying, the powder was sieved sequentially through 2 mm and 1 mm mesh sieves to ensure uniform particle size.

Table 1: Composition of CUR, PVP, and *β*-CD in each formulation.

	Curcumin	*β*-Cyclodextrin	PVP
Formulation 1	0.364 g	2.70 g	0.5% (0.015 g)
Formulation 2	0.364 g	2.70 g	1% (0.030 g)
Formulation 3	0.364 g	2.70 g	1.5% (0.045 g)

Determination of curcumin content by UV-VIS spectrophotometry

Quantification of CUR in inclusion complexes was analyzed spectrophotometrically using a Shimadzu UV-1800 Spectrophotometer (Shimadzu Corporation, Japan). Standard solutions of pure CUR were prepared in methanol at concentrations ranging from 0.3 to 7.2 µg/ml. The absorbance of the standard solutions was measured at 424 nm.

The quantification of curcumin in inclusion complex by UV-VIS spectrophotometry

To quantify the CUR content in the inclusion complex, 10 mg of the prepared complexes were dissolved in 100 mL of methanol, which was then filtered through a 0.45 MM membrane filter. The necessary dilutions were made, and the absorbance was measured using a UV-visible spectrophotometer.

Solubility studies

For this purpose, excessive amounts of the CUR and previously prepared three formulations were placed in glass test tubes separately, and distilled water was added to each tube to reach 2 ml. After shaking at

120 rpm in an aqueous shaker at 37ºC for 24 hours, the samples were centrifuged at 4000 rpm for 30 minutes. The upper solution was filtered through a 0.45 µm membrane filter, diluted with methanol, and the concentrations were calculated via UV- spectrophotometry (Pozharani et al., 2023).

Characterization studies of curcumin-loaded cyclodextrin complexes

Optical microscopy analysis

The surface morphologies of the physical mixture and CUR-loaded *β*-CD complexes were examined using an optical microscope (OLYMPUS-CX21FS1, Olympus Cor., Japan). Samples were mounted onto clean glass slides and observed under 45x magnification. Images were captured using a high-resolution Canon EOS R digital camera (Canon Inc., Japan).

For enhanced analysis, small fragments of the particles were compressed between two glass slides to create uniform layers, improving visibility. High-resolution images were processed with imaging software to extract detailed morphological features. This systematic approach provided valuable insights into the surface texture, particle size, and structural characteristics of CUR, the physical mixture, and their *β*-CD complexes (Patil et al., 2024).

Particle size distribution, polydispersity index, and zeta potential analysis

Freshly prepared formulations were diluted with distilled water, and their particle size and size distribution were analyzed using a Malvern Zetasizer (Malvern Panalytical Ltd., Malvern, UK) at 25°C. The measurement was conducted to ensure uniformity and consistency in the particle size of the formulations.

For zeta potential analysis, the aqueous suspensions were prepared at a specific concentration and assessed at 25°C using the same Malvern Zetasizer. The measurements utilized a 173°C detection angle to enhance the sensitivity of dynamic light scattering, providing accurate data on the surface charge and stability of the particles within the suspension (Mashaqbeh et al., 2021a).

***In-vitro* dissolution studies**

The dissolution profiles of CUR-*β*-CD: 1.5% PVP complex were compared to pure CUR to assess the impact of complexation on drug release behavior. Dissolution testing was conducted using a USP Type-II (paddle) dissolution apparatus (SOTAX, Switzerland). A 10 mg sample of CUR and an equivalent 10 mg of CUR from the chosen formulation were placed in 900 mL of deionized water at 37 ± 0.5°C, with stirring set at 100 rpm to simulate physiological conditions. For additional testing, simulated intestinal fluid (SIF) was prepared using phosphate buffer at pH 6.8 and 0.1% Tween 80 to replicate small

intestinal conditions. The volume of the dissolution medium was maintained at 900 mL, and the stirring speed was set to 100 rpm at 37°C. At predefined intervals (2, 6, 10, 15, 20, 30, 40, 60, 90, and 120 minutes), 5 mL aliquots were withdrawn using a syringe and filtered through a 0.45 μm PES disc filter. The samples were then appropriately diluted, and CUR concentration was analyzed using UV spectrophotometry. 5 mL of fresh medium was added after each withdrawal to maintain the dissolution medium volume. The experiments were conducted in triplicate to ensure the accuracy and reproducibility of the results (Hagbani and Nazzal, 2017; Jafar et al., 2020a; Mashaqbeh et al., 2021a).

Antibacterial activity

Determination of minimum inhibitory concentration (MIC)

The antimicrobial activities of CUR and its combination with *β*-CD were established by broth microdilution technique. The antibacterial activity was investigated against *Escherichia coli* ATCC 25922, *Staphylococcus aureus* ATCC 25923, *Enterococcus faecalis* ATCC 29212, and *Klebsiella pneumoniae* ATCC 700603. The inoculum of each bacterial strain was standardized to 1 x 10^6 cfu/mL, with the final sample concentrations varying from 4 to 0.125 mg/ml. The maximum concentration of samples in Mueller Hinton broth served as a negative control, whereas ciprofloxacin was employed as a positive control. Incubation was carried out for 18 hours at 37°C. The MIC was determined as the lowest concentration of the samples that inhibited the growth of each bacterial strain.

FTIR analysis of curcumin-cyclodextrin-PVP complexes

Infrared (IR) spectra of the formulation components, including pure CUR, β-CD, PVP, the physical mixture, and their supramolecular complex formulation, were recorded using a Shimadzu FTIR-8400s spectrophotometer (Japan). The formation of inclusion complexes was assessed by comparing the IR spectra of the solid complexes with those of the physical mixture containing an equivalent amount of curcumin.

To ensure consistency, the ratio of curcumin to potassium bromide (KBr) remained constant throughout the experiment. Accurately weighed samples and KBr were finely ground, mixed thoroughly, and compressed into pellets for spectrophotometric analysis. The spectra were scanned over a range of 4000–400 cm^{-1} at a resolution of 2 cm^{-1}, allowing for precise identification of functional group interactions and structural changes indicative of complex formation (Mohan et al., 2012; Zhang et al., 2016).

RESULTS AND DISCUSSION

The quantification of curcumin in inclusion complex by UV-VIS spectrophotometry

The calibration curve was established with a linear regression equation y=0.1642x−0.0035 and a high correlation coefficient (r2=0.9998). The spectrophotometric method's validation for the main parameters like assessing linearity, accuracy, precision, repeatability, the limit of detection (LOD), and the limit of quantification (LOQ) was conducted in accordance with International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use (ICH) guidelines. Accuracy was determined to be 95.73 ± 7.45%, and the linearity range was confirmed as 0.3–7.2 µg/ml. The LOD and LOQ values were calculated as 0.2236 µg/mL and 0.6776 µg/mL, respectively (Figure 3 and Table 2).

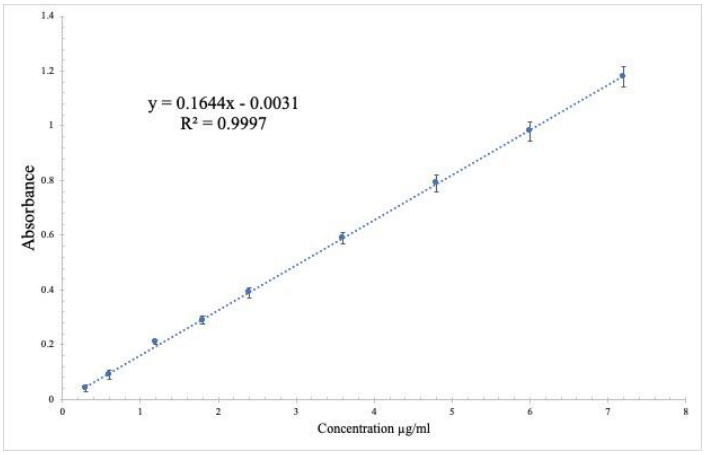


Figure 3: Calibration curve of curcumin.

Table 2: The spectrophotometric method's validation parameters.

Parameter	Value
Accuracy	95.73 ± 7.45
Slope	0.164
Intercept	0.003
Linearity range	0.3 – 7.2 µg/ml
Correlation coefficient (r)	0.999
SE of intercept	0.003
SD of intercept	0.011
LOD	0.224
LOQ	0.677

*SE: Standard Error SD: Standard Deviation; LOD: Limit of detection; LOQ: Limit of quantification.

Pursuant to the construction of the calibration curve, the concentration of CUR in each formulation was quantified via an assay. The recovery percentages illustrated in Figure 4 adhere to pharmacopeial standards.

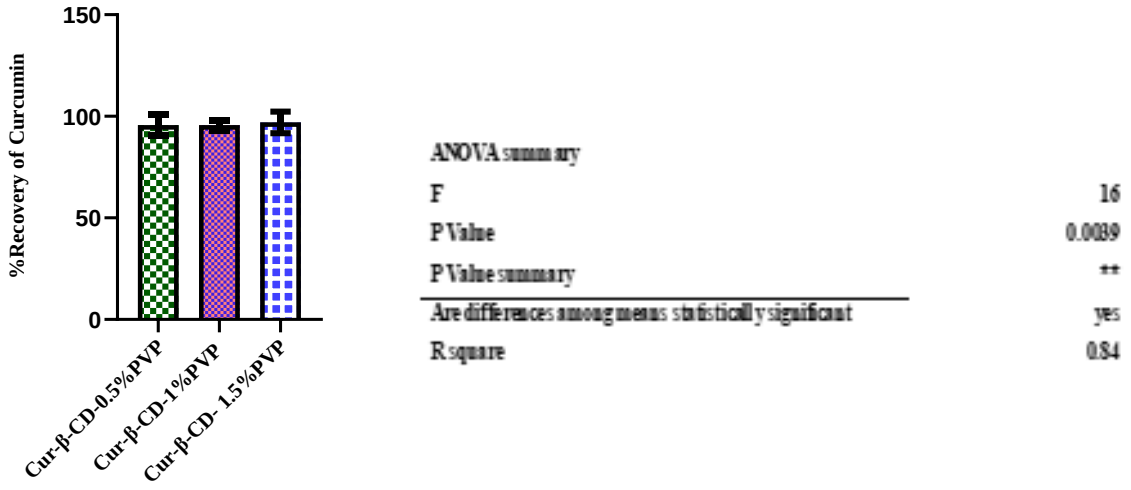


Figure 4: Recovery % of CUR-*β*-CD: 0.5% PVP ; CUR-*β*-CD: 1% PVP; CUR-*β*-CD-1.5% PVP.

Solubility studies

As shown in Figure 5, the aqueous solubility of pure CUR and the CUR-*β*-CD inclusion complex were measured and a notable 30-fold enhancement in CUR solubility through complexation was detected, confirming the 31-fold increase previously documented by Mangolim et al.(2014). The increased solubility of CUR upon the formation of the CUR-*β*-CD inclusion complex was further confirmed by UV-Vis spectroscopy, demonstrating a significant enhancement in solubility relative to pure CUR (Mangolim et al., 2014b). It has been noted that the sample with the highest PVP ratio demonstrated the most significant enhancement in solubility. Therefore, the CUR-*β*-CD: was 1.5% PVP used for further analysis (Jafar et al., 2020b).

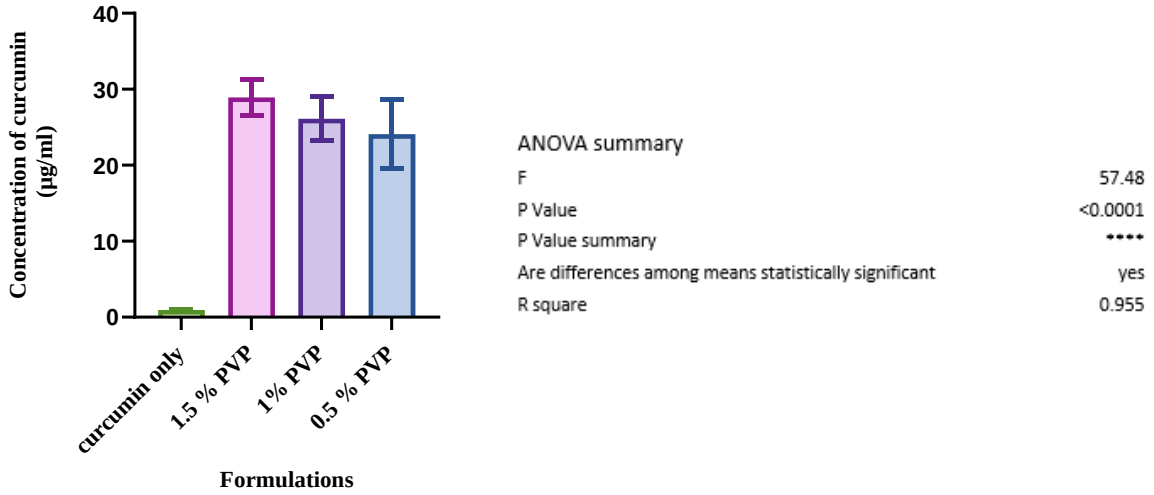


Figure 5: Solubility test of curcumin in comparison with three formulations.

Characterization studies of curcumin-loaded cyclodextrin complexes

Spectral insights from FTIR analysis of curcumin-cyclodextrin-PVP complexes

The FTIR spectra in Figure 6 illustrate the profiles of pure CUR, essential polymers (β-CD and PVP), their physical blends (1:1:1), and the selected formulation. The analysis identified characteristic peaks for CUR, including the phenolic O–H stretching vibration at 3505.6 cm^{-1}, the C=C stretching at 1628 cm^{-1}, the C=O and C=C vibrations at 1508.4 cm^{-1}, and the olefinic C–H bending vibration at 1427.6 cm^{-1}. These findings are all consistent with literature reports. For PVP, the presence of the C=O stretching band at 1650 cm^{-1} and CH_2 stretching vibrations between 2800–3000 cm^{-1} confirmed its polymer structure. Similarly, β-CD exhibited a broad O–H stretching peak between 3100–3500 cm^{-1}, an indicative of hydroxyl groups, and C–O–C stretching vibrations within 1020–1150 cm^{-1}, a characteristic of its ether linkages (Mangolim et al., 2014a; Rahma et al., 2016).

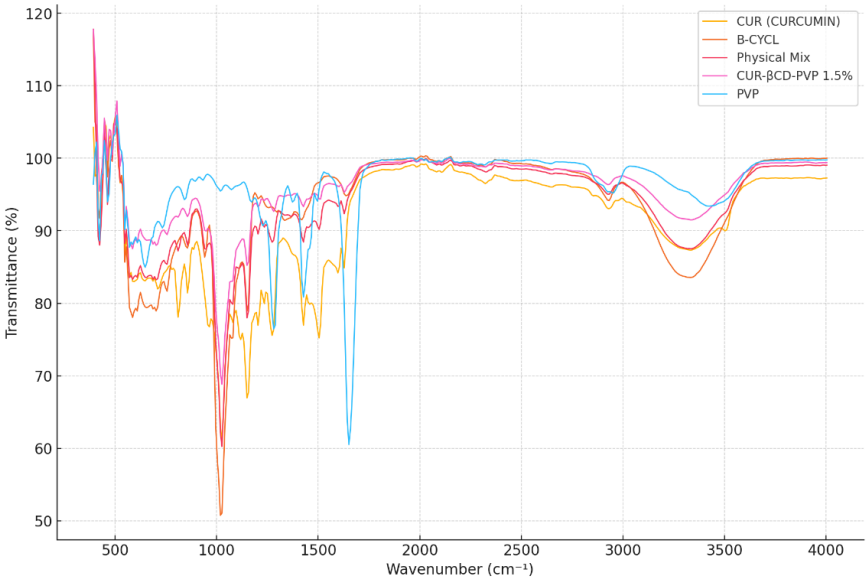


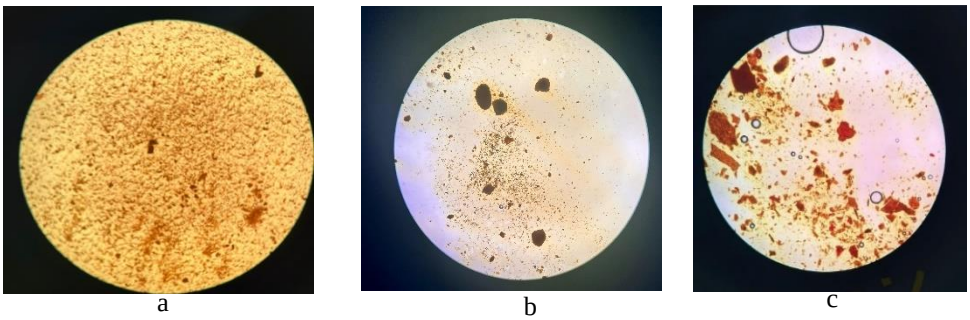
Figure 6*:* FT-IR spectrum of CUR, *β-CD,* PVP, drug-polymer physical mixture (1:1:1, w/w/w) and selected formulation.

The physical mixture displayed a combined spectrum featuring peaks from CUR, *β*-CD, and PVP. A slight weakening of CUR's characteristic peaks was observed in the physical blend and the formulation, likely due to the dilution effect of the polymers. However, the absence of significant peak shifts suggests no notable chemical interactions occurred between the drug and polymers in these preparations.

Optical microscopy analysis

The optical microscopy analysis revealed distinct differences in the surface morphology among CUR, physical

mixture, and CUR-loaded *β*-CD complexes. CUR appeared as irregularly shaped crystalline particles while the physical mixture displayed a heterogeneous composition with separate regions of CUR and *β*-CD. In contrast, the cyclodextrin complexes exhibited a more uniform and smoother surface texture, indicating the successful inclusion of CUR within the cyclodextrin cavities (Figure 7). These observations suggest a significant alteration in the physical properties of CUR upon complexation, which may enhance its solubility and stability for potential pharmaceutical applications (Yallapu, 2010).



a b c

Figure 7: Images of a) Pure CUR b) Physical mixture c) CUR-*β*-CD: 1.5 %PVP.

Particle size, polydispersity index (PDI) and zeta potential

The particle size analysis revealed that the average particle size of the prepared formulations was 463.6 ± 30.19 nm, with a PDI of 0.472. These values suggest a moderate particle size distribution, indicating homogeneity in the formulation. The relatively small particle size aligns with expectations for enhanced drug delivery potential, particularly for topical applications, as smaller particles are associated with improved penetration and absorption. The smaller particle size observed in this study compared to typical cyclodextrin complexes could be attributed to factors like aggregate formation or the preparation method, highlighting the impact of formulation techniques on the final characteristics (Figure 8).

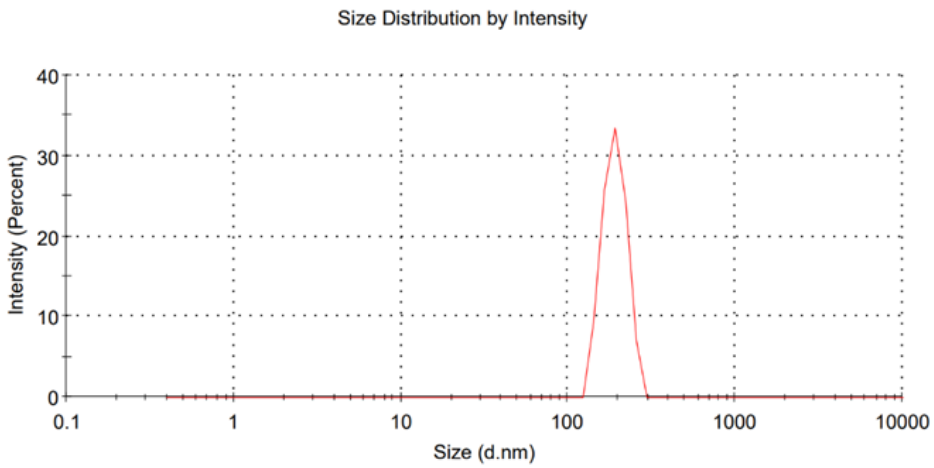


Figure 8: Size distribution by intensity of the CUR-*β*-CD: 1.5%.PVP.

The zeta potential measurements yielded a value of -13.3 ± 5.56 mV, indicating a negative surface charge (Figure 9). This result suggests that the formulation has modest electrostatic stability. The obtained zeta potential value implies that the formulation demonstrates adequate stability under the tested conditions. This finding is in agreement with a previous study which reported a similar trend in zeta potential values, highlighting the impact of cyclodextrin complexation on surface charge and stability (Mashaqbeh et al., 2021a).

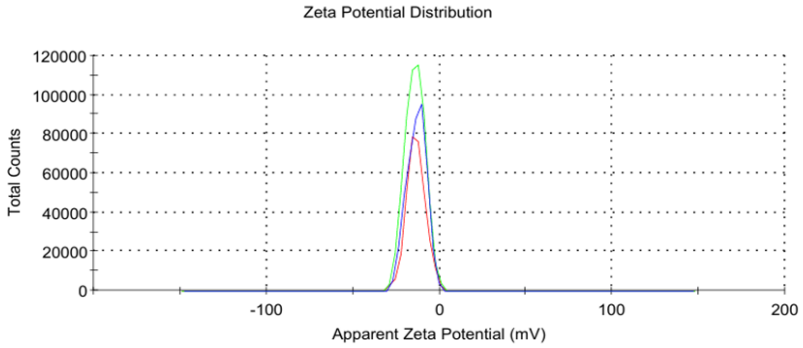


Figure 9: Zeta potential distribution of CUR-*β*-CD-1.5%.PVP.

These findings underscore the critical role of particle size, PDI, and zeta potential in determining the stability and functional performance of the formulations. Further studies are warranted to correlate these physicochemical properties with drug release profiles and therapeutic outcomes (Darandale and Vavia, 2013; Mashaqbeh et al., 2021b; Serri et al., 2017).

Dissolution studies

The in vitro dissolution profiles of CUR and the selected CUR-*β*-CD: %1.5 PVP complex, prepared using the kneading technique, demonstrates a superior enhancement in CUR's release (Figure 10).

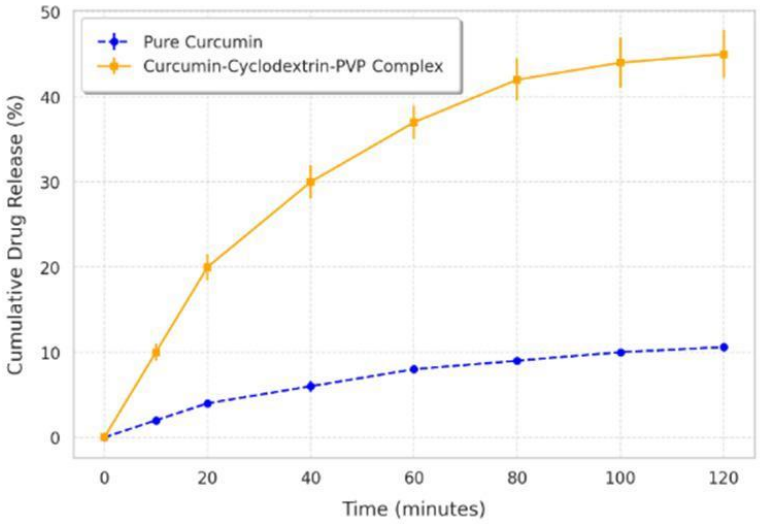


Figure 10: Comparative drug release profile of pure CUR and the CUR-*β*-CD-1.5% PVP in simulated intestinal fluid (pH 6.8) over 120 minutes.

The drug release profile of pure CUR demonstrated minimal release over 120 minutes, which can be attributed to its inherent poor aqueous solubility and strong hydrophobicity at near-neutral pH. Conversely, the *β*-CD-PVP inclusion complex showed significantly enhanced drug release, indicating the efficacy of this formulation in improving CUR's solubility and dissolution rate in a basic medium.

The enhancement in the release can be attributed to multiple factors: the ability of β-CD to encapsulate hydrophobic molecules, thereby increasing CUR's wettability and reducing its crystalline nature, and the auxiliary effect of PVP which acts as a solubilizing agent and further improves the dispersibility of the drug complex in the aqueous medium. Additionally, the greater ionization of the phenolic groups at pH 6.8 further enhances the solubility and release of CUR from the inclusion complex by increasing its hydrophilicity and reducing aggregation tendencies. These effects collectively reduce the thermodynamic barriers to dissolution.

This observed improvement highlights the potential of the *β*-CD-PVP inclusion system as a robust formulation strategy to address the solubility limitations of CUR under physiological pH conditions. Such advancements are crucial for developing efficient delivery systems for CUR, particularly for applications in topical or oral drug delivery systems (Hassan, 2018; Jafar et al., 2020a; Rezaei and Nasirpour, 2019).

Antibacterial activity of curcumin alone and in combination with cyclodextrin and PVP

In order to assess the antimicrobial activities associated with the CUR and CUR-β-CD combination, the microdilution

method was used to measure the MIC against *E. faecalis*, *S. aureus*, *E. coli*, and *K. pneumoniae* (Table 3). CUR revealed selective activity against Gram-positive bacteria including *S. aureus* (0.25 mg/mL) and *E. faecalis* (0.125 mg/mL). Furthermore, CUR, when combined with β-CD, demonstrated higher antibacterial activity with an MIC of 0.25 mg/ml against *S. aureus* and 0.0625 mg/ml against *E. faecalis*. However, no activity was observed against Gram negative bacteria (*E. coli*, and *K. pneumoniae).* This could be due to the structural difference in the cell wall of Gram positive and Gram negative bacteria. The outer lipopolysaccharide membrane found in Gram negative bacteria may act as a barrier for compounds containing antibacterial activity, making them intrinsically impermeable (Liscano et al., 2019).

Table 3: MIC of curcumin alone and in combination with cyclodextrin against Gram-negative and Gram-positive bacteria.

Agents		Gram positive bacteria		Gram negative bacteria	
		S. aureus **ATCC 25923**	***E. faecalis*** **ATCC 29212**	***E. coli*** **ATCC 25922**	***K. pneumoniae*** **ATCC 700603**
Sample (mg/mL)	Curcumin	0.25 ± 0	0.125 ± 0	>4	>4
Sample (mg/mL)	Curcumin +*β*- CD*	0.125 ± 0	0.0625	>4	>4
Control (mg/L)	Ciprofloxacin	0. 25 ± 0	1 ± 0.083	0.008 ± 0	0.25 ± 0.021

Data represented as the standard error of the mean (±S.E.M).
*CD-cyclodextrin.

CONCLUSION

The inclusion complexes of CUR with *β*-CD and PVP markedly improved the solubility and bioavailability of curcumin, mitigating its principal constraints as a medicinal agent. The improved formulation, including 1.5% PVP, exhibited a significant 30-fold enhancement in solubility, confirmed by UV-visible spectrophotometry and particle size characterization. The improved dissolving profiles and antimicrobial tests highlighted the effectiveness of these complexes, especially against Gram positive bacteria, including *S. aureus* and *E. faecalis*. The findings underscore the efficacy of *β*-CD and PVP inclusion complexes as delivery methods for curcumin, facilitating its broader utilization in pharmaceutical and biological domains. Subsequent studies may examine the practical application of the results and assess other functional characteristics of the formed complexes.

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Review Article: Integral Role of Physics in Advancing Pharmacy Education and Research

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Abstract

Physics plays a fundamental role in advancing pharmacy education and research, providing theoretical underpinnings and practical tools necessary to address complex challenges in drug development, delivery, and diagnostics. This review explores the integration of physics into the pharmacy curriculum, highlighting how principles such as fluid dynamics, thermodynamics, and spectroscopy (Tokgoz and Sakalli, 2018) enhance students' critical thinking and problem-solving skills. Additionally, it examines the pivotal contributions of physics to pharmaceutical research, including molecular modeling, imaging technologies like MRI and PET, and nanotechnology-driven drug delivery systems. Despite challenges in interdisciplinary collaboration and resource allocation, innovative teaching strategies and laboratory-based learning are shown significant promise. Looking forward, the convergence of artificial intelligence and physics, as highlighted by recent Nobel Prize achievements in attosecond physics and bioorthogonal chemistry, is set to revolutionize pharmaceutical sciences, offering unprecedented precision and efficiency in drug discovery and personalized medicine.

Keywords

Artificial intelligence, diagnostic technologies, drug delivery, molecular modeling, pharmacy education, physics.

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INTRODUCTION

Physics serves as a universal language for understanding and describing the fundamental laws of nature. Its principles permeate nearly every scientific discipline, offering a critical lens through which we explore complex phenomena. In the context of pharmacy, physics provides a foundational framework for numerous processes, ranging from drug formulation to delivery mechanisms and diagnostic technologies (Dhina et al., 2023; McCall, 2007). Despite its fundamental role, the explicit integration of physics into pharmacy education is often limited, with greater emphasis placed on chemistry and biological sciences. This oversight can obscure the value of physics as a key contributor to pharmaceutical advancements (Erdogan et al., 2021).

The historical evolution of pharmacy education has largely centered on the chemical and biological aspects of drug development, with physics playing a secondary role (Pillai and Cummings, 2013). However, as modern healthcare becomes increasingly reliant on interdisciplinary approaches, the importance of physics has grown exponentially. Drug design, for instance, is deeply rooted in physical chemistry, encompassing the study of molecular interactions, thermodynamics, and kinetics (Wilkinson et al., 2004). Similarly, the development of innovative drug delivery systems-such as nanoparticles and liposomes-requires an intricate understanding of mechanical forces, surface tension, and fluid dynamics (Blanke and Blanke, 1984).

Beyond its applications in drug formulation and delivery, physics also underpins critical diagnostic technologies that have revolutionized modern medicine. Techniques such as magnetic resonance imaging (MRI), computed tomography (CT), and positron emission tomography (PET) rely on principles of nuclear physics and electromagnetism (McCall, 2007; Gulcan et al., 2021). These technologies not only aid in early disease detection but also enhance our understanding of physiological processes, paving the way for more targeted and effective treatments (Pepeu and Giovannini, 2009).

From a pedagogical perspective, integrating physics into pharmacy education can significantly enhance students' problem-solving and analytical skills (Dhina et al., 2023). The study of physics trains individuals to approach problems systematically, breaking down complex systems into comprehensible components (Erdogan et al., 2021). For pharmacy students, this skillset is invaluable in

navigating the multifaceted challenges of drug development, quality control, and clinical application (Gulcan et al., 2019). However, achieving this integration requires a paradigm shift in how physics is taught within the pharmacy curriculum (Wilkinson et al., 2004). Traditional lecture-based methods must be supplemented with context-driven approaches that highlight the relevance of physics to pharmaceutical sciences (Shukur et al., 2021).

Several studies have highlighted the potential benefits of such an integrated approach. For instance, the use of case studies that link physics concepts to real-world pharmaceutical problems has been shown to improve student engagement and comprehension (Ellman, 1958). Laboratory experiments, too, can serve as a powerful tool for demonstrating the practical applications of physics, from measuring drug solubility and diffusion rates to analyzing the mechanical properties of tablet formulations (Blanke and Blanke, 1984; McCall, 2007).

Despite these advantages, significant barriers remain. One of the primary challenges is the lack of interdisciplinary collaboration between physics and pharmacy departments (Gulcan et al., 2003). Bridging this gap requires concerted efforts to develop curricula that are both scientifically rigorous and practically relevant (Pepeu and Giovannini, 2009). Additionally, faculty development programs can play a crucial role in equipping educators with the skills needed to effectively teach physics in a pharmaceutical context (Pillai and Cummings, 2013; Wilkinson et al., 2004).

In conclusion, physics is not merely a supplementary discipline in pharmacy education but a cornerstone for understanding and advancing the pharmaceutical sciences (Erdogan et al., 2021). As the healthcare landscape continues to evolve, the integration of physics into pharmacy education will be essential for preparing the next generation of pharmacists to meet the demands of an increasingly complex and interdisciplinary field (Gulcan et al., 2021).

The review paper is organized as follows. Section 2 elaborates on how foundational physics concepts are integral to understanding drug formulation and delivery mechanisms, supported by examples and measurable learning outcomes. In section 3, the applications of physics in cutting-edge research, including molecular modeling, nanotechnology, and diagnostic imaging, are discussed with real-world implications. Section 4 highlights the need for innovative teaching methods, interdisciplinary collaboration, and laboratory-based learning to effectively incorporate physics into pharmacy

education. The review concludes with section 5, which is a summary of the key findings, emphasizing the future directions for integrating artificial intelligence and recent advances in physics, such as attosecond technologies, to revolutionize pharmaceutical sciences.

IMPORTANCE OF PHYSICS IN PHARMACY EDUCATION

Physics serves as the backbone for numerous applications in pharmacy education, providing fundamental insights into the physical principles governing pharmaceutical systems. From understanding drug solubility to designing advanced diagnostic tools, the role of physics cannot be overstated. This section highlights the importance of physics in the pharmacy curriculum, discussing key concepts, formulas, and real-world examples that underline its relevance.

One of the most direct applications of physics in pharmacy is the study of fluid dynamics. Fluid flow is critical in understanding how drugs disperse in the human body, particularly through the circulatory and lymphatic systems (McCall, 2007; Wilkinson et al., 2004). For instance, Poiseuille's Law, which governs laminar flow, can be expressed as:

$$Q = \pi r^4 \Delta P \,/\, (8\mu L)$$

Here, Q represents the flow rate, r is the radius of the tube (e.g., blood vessel), ΔP is the pressure difference, μ is the viscosity, and L is the length of the tube. This equation highlights how minor changes in the radius of blood vessels can significantly impact the flow rate, which is a critical consideration for intravenous drug delivery.

Thermodynamics, another essential branch of physics, provides theoretical framework for understanding drug stability and solubility. The Gibbs free energy (ΔG) equation (Pourhassan et al., 2023), often used in pharmaceutical studies, is given as:

$$\Delta G = \Delta H - T\Delta S$$

This equation helps predict whether a reaction or process will occur spontaneously (Dhina et al., 2023; Erdogan et al., 2021). For example, the solubility of a drug in a solvent depends on the interplay between enthalpy (ΔH) and entropy (ΔS) changes, influencing formulation strategies and storage conditions.

Physics also plays a pivotal role in the design and optimization of medical imaging technologies, such as MRI and CT (Blanke and Blanke, 1984; Gulcan et al., 2021). MRI, for instance, relies on principles of nuclear magnetic resonance. The Larmor frequency, which describes the procession of nuclear spins in a magnetic field, is expressed as:

$$\omega = \gamma B$$

Here, ω is the angular frequency, γ is the gyromagnetic ratio, and B is the magnetic field strength.

Spectroscopic techniques such as ultraviolet-visible (UV-Vis) and infrared (IR) spectroscopy are foundational in pharmaceutical analysis. The Beer-Lambert law is widely used to determine the concentration of drug solutions and is expressed as:

$$A = \varepsilon c l$$

In this equation, A represents absorbance, ε is the molar absorptivity, c is the concentration of the solution, and l is the path length of the light through the sample. This law is critical for ensuring accurate dosage in liquid formulations.

Rheology, the study of flow and deformation of matter, is integral to the development of various pharmaceutical dosage forms such as creams, ointments, and gels (Pepeu and Giovannini, 2009; McCall, 2007). Understanding the shear-thinning or shear-thickening behavior of these formulations ensures their stability and efficacy. For instance, shear-thinning behavior, where viscosity decreases with increasing shear rate, is critical for injectable formulations, enabling ease of administration through syringes.

To summarize, physics is a cornerstone of pharmacy education, providing the theoretical and practical tools necessary to address complex pharmaceutical problems. By integrating physics concepts into the curriculum, educators can empower future pharmacists to innovate and excel in their field (Blanke and Blanke, 1984; Erdogan et al., 2021).

ROLE OF PHYSICS IN ADVANCED PHARMACEUTICAL RESEARCH AND TECHNOLOGY

Physics plays a transformative role in pharmaceutical research, bridging the gap between theoretical principles and practical applications. The incorporation of physics into research has enabled significant advancements in drug discovery, formulation, delivery mechanisms, and diagnostic technologies. This section explores the pivotal role of physics in pharmaceutical research, highlighting key concepts, equations, and real-world applications.

One of the foundational applications of physics in pharmaceutical research is the study of molecular interactions using quantum mechanics. Techniques such as molecular docking and simulations rely on the Schrödinger equation to predict the behavior of molecules at the atomic level.

The time-independent form of the Schrödinger equation is given as:

$$H\Psi = E\Psi$$

Here, H is the Hamiltonian operator representing the total energy of the system, Ψ is the wave function, and E is the energy eigenvalue. By solving this equation, researchers can predict molecular conformations and interactions, guiding the development of more effective drug candidates (Erdogan et al., 2021; Gulcan et al., 2021).

Thermodynamics also plays a crucial role in understanding drug stability and solubility. The van 't Hoff equation, used to analyze the temperature dependence of equilibrium constants, is expressed as:

$$ln(K) = -\Delta H/RT + C$$

In this equation, K is the equilibrium constant, ΔH is the enthalpy change, R is the gas constant, T is the temperature, and C is a constant. Understanding this relationship allows researchers to optimize conditions for drug formulations, ensuring their stability and efficacy (Wilkinson et al., 2004; Blanke and Blanke, 1984).

The study of fluid dynamics is indispensable in designing drug delivery systems. The Navier-Stokes equations describe the motion of viscous fluids, which is critical for understanding blood flow and drug dispersion. A simplified version of these equations for incompressible flow is:

$$\rho(\partial v/\partial t + v \cdot \nabla v) = -\nabla p + \mu\nabla^2 v$$

Here, ρ is the fluid density, v is the velocity vector, p is the pressure, and μ is the dynamic viscosity. These equations are used to model the behavior of injectable drugs and predict their distribution within the body (McCall, 2007; Dhina et al., 2023).

Physics also contributes to nanotechnology-based drug delivery systems. The application of optical tweezers, which relies on the principles of electromagnetic radiation pressure, has facilitated the manipulation of nanoparticles for targeted drug delivery. The trapping force in optical tweezers is given by:

$$F = (nP/c)(1 + R - T)$$

In this equation, F is the force, n is the refractive index, P is the power of the laser beam, c is the speed of light, R is the reflectivity, and T is the transmissivity. Such technologies enhance precision in delivering drugs to specific sites, minimizing side effects (Gulcan et al., 2019; Ellman, 1958).

Imaging technologies have also benefited from advancements in physics. PET and MRI are vital tools in pharmaceutical research, enabling non-invasive monitoring of drug behavior within the body. The

signal-to-noise ratio (SNR) in MRI, a critical parameter for image quality, is influenced by the following relationship:

$$SNR \propto B_0{}^2\sqrt{(\Delta V)}$$

Here, B_0 is the magnetic field strength, and ΔV is the voxel volume. Higher B_0 fields improve image resolution, allowing detailed observation of drug interactions and effects (Pepeu and Giovannini, 2009; Shukur et al., 2021).

To summarize, physics underpins a wide range of innovations in pharmaceutical research, from molecular modeling to advanced imaging techniques. Its principles provide the tools to address complex challenges, paving the way for more effective drugs and delivery systems (Erdogan et al., 2021; McCall, 2007).

INTEGRATION OF PHYSICS INTO PHARMACY CURRICULUM

Integrating physics into the pharmacy curriculum is essential to equipping students with the foundational knowledge and critical thinking skills required to address complex challenges in pharmaceutical sciences. By understanding key physical principles, pharmacy students gain insights into drug formulation, delivery mechanisms, and diagnostic technologies. This section explores the strategies and outcomes associated with integrating physics into the pharmacy curriculum, along with examples of learning outcomes and real-world applications.

Physics courses tailored for pharmacy students should emphasize the relevance of physical principles to pharmaceutical applications. For instance, understanding thermodynamics can help students predict drug stability under various conditions, while knowledge of fluid dynamics can aid in modeling blood flow and drug dispersion. These concepts are critical in both clinical and research settings (McCall, 2007; Erdogan et al., 2021).

A well-structured curriculum should also focus on measurable learning outcomes. Examples of physics-related learning outcomes for pharmacy students include:

1. Demonstrating an understanding of the principles of fluid dynamics and their application to blood flow and intravenous drug delivery.
2. Applying thermodynamic principles to evaluate drug solubility, stability, and shelf life.
3. Utilizing spectroscopic techniques, such as UV-Vis and IR spectroscopy, to analyze pharmaceutical formulations.
4. Explaining the role of nuclear physics in medical imaging technologies, including MRI and PET scans.

5. Modeling molecular interactions using quantum mechanics to predict drug efficacy and receptor binding.

Innovative teaching methods, such as problem-based learning (PBL) and case studies, can enhance the integration of physics into the pharmacy curriculum. For instance, PBL activities could involve analyzing the diffusion of a drug through a semipermeable membrane or designing a nanoparticle-based drug delivery system (Shukur et al., 2021; Gulcan et al., 2021). Such approaches encourage active learning and help students connect theoretical knowledge to practical applications.

The use of laboratory experiments is another effective way to teach physics in the context of pharmacy. Examples of experiments include measuring the diffusion coefficients of drug molecules, analyzing fluid viscosity, and investigating the thermal properties of pharmaceutical materials. These hands-on experiences not only reinforce theoretical concepts but also prepare students for real-world challenges in research and clinical practice (Dhina et al., 2023; Wilkinson et al., 2004).

Assessment strategies should also be aligned with the integration of physics into the pharmacy curriculum. Traditional exams can be supplemented with project-based assessments that require students to solve complex, interdisciplinary problems. For example, a project could involve designing a drug delivery system that considers fluid dynamics, thermodynamics, and material properties (Blanke and Blanke, 1984; Pepeu and Giovannini, 2009).

Despite its importance, the integration of physics into the pharmacy curriculum faces several challenges. These include a lack of interdisciplinary collaboration between departments, limited faculty expertise in physics, and insufficient resources for laboratory-based instruction. Addressing these challenges requires institutional support, faculty development programs, and investments in state-of-the-art teaching facilities (Ellman, 1958; Pal et al., 2023).

In conclusion, integrating physics into the pharmacy curriculum is vital for developing the analytical and problem-solving skills necessary for success in pharmaceutical sciences. By adopting innovative teaching strategies and aligning learning outcomes with industry needs, educators can prepare the next generation of pharmacists to excel in both academic and clinical settings (Erdogan et al., 2021; McCall, 2007).

CONCLUSION

This review has explored the multifaceted role of physics in pharmacy education and research, emphasizing its foundational importance in understanding and advancing

pharmaceutical sciences. Physics provided the theoretical and practical frameworks necessary for addressing challenges in drug design, delivery, diagnostics, and education. In pharmacy education, physics was integrated to equip students with critical thinking skills and interdisciplinary knowledge. By learning key principles such as fluid dynamics, thermodynamics, and spectroscopy, students gained a comprehensive understanding of drug stability, solubility, and delivery mechanisms. Laboratory experiments and PBL further reinforced these principles, connecting theory to practical applications.

In pharmaceutical research, the application of physics was shown to bridge the gap between theoretical models and clinical outcomes. From the Schrödinger equation guiding molecular docking to the Navier-Stokes equations modeling fluid flow, physics was instrumental in innovating drug delivery systems, imaging technologies, and nanotechnology-based approaches. Imaging modalities such as MRI and PET relied on physical principles, enhancing the precision of diagnostics and treatment monitoring. Furthermore, techniques like optical tweezers and spectroscopy enabled targeted drug delivery and analysis, minimizing side effects and optimizing therapeutic efficacy.

Integrating physics into the pharmacy curriculum faced challenges, including the need for interdisciplinary collaboration and resources. Despite these hurdles, the adoption of innovative teaching strategies, such as PBL and laboratory-based instruction, was demonstrated to significantly enhance the educational experience. These approaches not only prepared students for research and clinical practice but also cultivated a deeper appreciation of the relevance of physics in their professional roles.

Looking ahead, the integration of artificial intelligence (AI) into the intersection of physics and pharmacy presents transformative potential. AI algorithms, particularly those leveraging advancements in quantum computing, are expected to revolutionize molecular modeling, drug discovery, and personalized medicine. The 2024 Nobel Prize in Physics (Hopfield and Hinton, 2024) highlighted breakthroughs in attosecond physics, which promise to refine imaging techniques and drug-target interactions at unprecedented temporal resolutions. Similarly, the Nobel Prize in Chemistry (Baker et al., 2024) celebrated advancements in bioorthogonal chemistry, which, when coupled with AI-driven insights, could lead to more precise and dynamic pharmaceutical interventions.

The future of this field will likely involve a deeper integration of AI and physics, creating new paradigms in pharmaceutical sciences. By harnessing the computational

power of AI, researchers can accelerate the development of drugs and diagnostics, optimize delivery mechanisms, and predict patient-specific outcomes with greater accuracy. This confluence of disciplines will not only enhance the effectiveness of therapeutic interventions but also redefine the educational frameworks that prepare future pharmacists for this rapidly evolving landscape.

DECLARATION

I, Izzet Sakalli, hereby declare that this manuscript is my original review article and has not been published or submitted elsewhere in any form. I confirm that all sources used in the preparation of this article have been appropriately cited and referenced. There is no conflict of interest related to the publication of this work. I take full responsibility for the accuracy of the content and conclusions presented in this manuscript. Additionally, I acknowledge that the research and analysis presented in this paper align with ethical standards and academic integrity.

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