ejpmr, 2025, 12(5), 774-780

SJIF Impact Factor 7.065

EUROPEAN JOURNAL OF PHARMACEUTICAL AND MEDICAL RESEARCH

www.ejpmr.com

Research Article

ISSN 2394-3211

EJPMR

SUSTAINABLE PRODUCTION OF METHYL SALICYLATE: UTILIZING *BETULA PAPYIFERA* EXTRACT IN GREEN SYNTHESIS

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Article Received on 26/03/2025 **Article Revised on 16/04/2025** **Article Published on 06/05/2025**

ABSTRACT

Background The increasing demand for sustainable and eco-friendly production processes has sparked interest in green chemistry approaches. *Betula papyrifera*, also known as paper birch, contains salicin, a glycoside that can be transformed into salicylic acid, a precursor to Methyl Salicylate. This study investigates the potential of using *Betula papyrifera* extract in a green synthesis pathway for Methyl Salicylate production, presenting a promising alternative to conventional methods. **Result** A groundbreaking method for synthesizing Methyl Salicylate using birch bark powder as a natural catalyst has delivered outstanding results with a 95% yield and purity achieved in just 5 minutes. This approach demonstrates significant environmental benefits and showcases the compound's desired properties and heightened biological activity through IR spectroscopy and antimicrobial/antifungal activity assays. **Conclusion** This new way to make Methyl Salicylate is a great example of using natural catalysts and microwave technology to be more efficient and eco-friendly. It sets a new standard for being sustainable and can be used in green chemistry and industry.

KEYWORDS: Green Chemistry, Sustainable Production, *Betula papyrifera*, Eco-friendly, IR spectroscopy.

INTRODUCTION

Green Chemistry represents a modern approach to chemical design, emphasizing safety and sustainability. It prioritizes the development of products and processes that minimize harm to humans and the environment, while also promoting eco-friendly alternatives. This innovative approach is guided by a set of principles, such as innovating for safety, using renewable resources, avoiding hazardous chemical synthesis, and minimizing energy consumption. These principles aim to revolutionize the industry with cleaner, healthier solutions.

Betula to Betulin

Betula papyifera, also known as paper birch, contains betulin in its bark. We have discovered a new method to extract salicin from the bark and convert it into salicylic acid. This process enables us to produce methyl salicylate, which has various practical applications. Our method is not only more environmentally friendly due to the use of a renewable source but also more economical. Furthermore, betulin possesses properties that could be beneficial in the development of new medications, skincare items, and dietary supplements.

AIM

Sustainable production of methyl salicylate utilizing *Betula papyifera* extract in green synthesis.

OBJECTIVE

1. Improve enzymatic extraction of salicin.
2. Develop a Microwave-assisted esterification protocol.
3. Characterize the synthesized Methyl salicylate.

MATERIALS

In an innovative approach to synthesizing methyl salicylate, I leveraged a combination of traditional and modern techniques. I employed birch bark powder as the starting material, harnessing the power of microwave oven extraction to isolate salicylic acid. Infrared (IR) spectroscopy was utilized to identify the characteristic functional groups of methyl salicylate, while pH measurements were taken to determine the optimal conditions. Thin Layer Chromatography (TLC) enabled the detection and separation of salicylic acid and methyl salicylate, and solubility tests were conducted to further characterize the compounds. This multifaceted approach allowed for a comprehensive understanding of the synthesis process.

METHODS

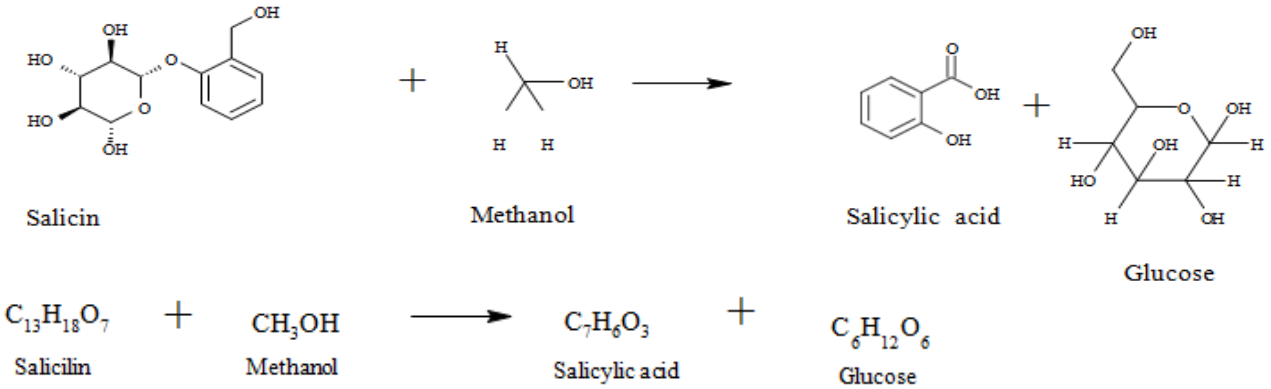
Extraction of Salicylic Acid from Birch bark powder by using the microwave oven

Table 1

Materials	Extraction of salicylic acid (quantities)
Birch bark powder	2 g
Methanol	10ml
Time	30-60 seconds
Temperature	60-80˚c
Microwave power	150-250 watt

Fig. 1: Salicylic Acid is Extracted from birch bark powder.

Chemical structure



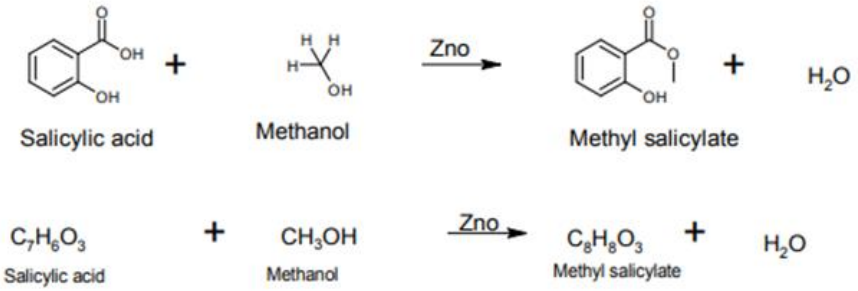
Green synthesis of Methyl salicylate by using the microwave oven

Table 2

Materials	Green synthesis of methyl salicylate (quantities)
Extracted salicylic acid	2 grams
Methanol	10ml
Zinc oxide	0.5 grams
Time	30-60 seconds
Temperature	60-80˚c
Microwave power	150-250 watt

Fig. 2: Extracted salicylic acid from birch bark powder is converted into Methyl salicylate.

Chemical structure for Methyl salicylate



Theoretical yield calculation

1. Mass of salicylic acid into moles:

Moles of salicylic acid = mass/molecular weight = 2g/138.12g/mol = 0.0145 mol

2. Calculate the theoretical moles of methyl salicylate:

Moles of methyl salicylate = moles of salicylic acid = 0.0145mol

Theoretical mass = moles ×molecular weight = 0.0145 mol ×152.15g/mol = 2.21 g

Yield calculation

Practical yield = 2.10grams

Theoretical yield = 2.21 grams

Percentage % = (Practical yield /Theoretical yield) × 100

(2.10g /2.21g) × 100 =0.950 × 100 = 95%

Physical characterization

1. TLC was to Evaluate the salicylic acid and methyl salicylate

- The Mobile phase for salicylic acid: Chloroform: Methanol (9:1)
- The Mobile phase for methyl salicylate: Hexane: Ethyl acetate (8:2)

2. Solubility test for Methyl salicylate

- Prepare a small amount of methyl salicylate about 2g.
- Add a small amount of each solvent about 5ml to separate the test tube.
- Add a few grains of methyl salicylate to each test tube.
- Stir or shake the mixture to observe the solubility.
- Record the result.

3. pH determination of methyl salicylate

- Prepare a solution of methyl salicylate in distilled water.
- Dip the pH electrode into methyl salicylate solution.
- Wait for the pH reading to stabilize
- Repeat the process three times to get the average value.

4. Qualitative chemical test for salicylic acid Ferric chloride test

- Prepare a 1% solution of ferric chloride in water.
- Dissolve the salicylic acid in a small amount of water or methanol.
- Add a few drops of Fecl3 solution into the sample solution.
- Purple or violet color to indicate the presence of salicylic acid.
- The intensity of color is proportional to the quantity of salicylic acid present.

5. Anti-microbial activity for *staphylococcus aureus*

- Mix 1g of agar powder with 50ml of water, heat, and pour into petri dishes.
- Add bacteria to the mixture and spread evenly.
- Let it cool, then make small holes in the agar.
- Mix methyl salicylate with ethanol and carefully add it into the holes.
- Let it sit at 37°c for 24 hours.
- Measure the clear area of the holes to see how well the methyl salicylate stopped the bacteria from growing.

6. Anti-fungal activity of *candida albicans*

- Mix 0.4g peptone, 0.8g dextrose, and 0.4g agar in a clean container with 20ml water.
- Heat and sterilize the mixture, then let it cool to 50-60℃
- Pour the mixture into petri dishes and add bacteria from a previous culture.
- Let it solidify, then make small holes in the agar.
- Dissolve methyl salicylate in ethanol and add it to the holes using a clean pipette.
- Let it sit at 37°c for 24 hours.
- Measure the clear area around the holes to see how well the methyl salicylate stopped the bacteria from growing.

RESULTS

Colour: Brown

Odor: Aromatic

Melting point: 150-161°c (318-322°c)

1 Solubility

Water: Insoluble (very slightly soluble) Ethanol (95%): soluble

Acetone: soluble Dichloromethane (DCM): soluble

Hexane: Insoluble (sightly soluble)

Table 3

Compound	Mol. Weight (g/mol)	Mol. Formula	Percentage yield (%)	Rf value
Green synthesis of methyl salicylate	152.1494	C8H803	95	0.67
Salicylic acid	138.1	C7H6O3	95	0.47

2. Solubility test for methyl salicylate

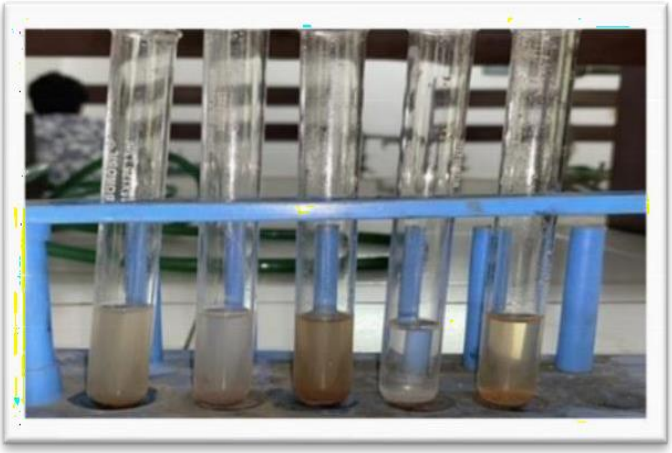


Fig. 3: Solubility Test for Methyl Salicylate.

3. Determination of pH

Fig. 4: pH value 9.00 for Methyl Salicylate.

4. Qualitative chemical test for salicylic acid

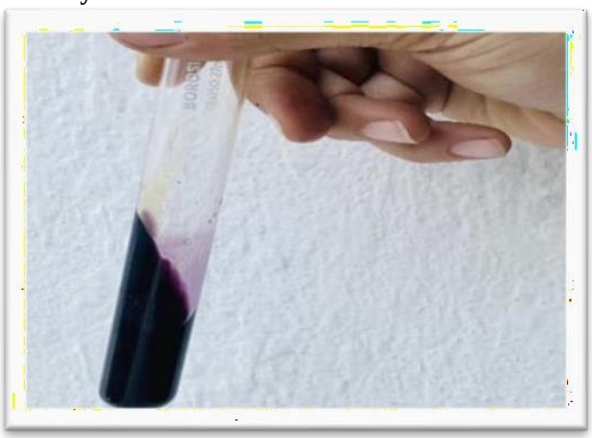


Fig. 5: Qualitative chemical test for extracted salicylic acid occurs purple color indicates the presence of salicylic acid.

5. Anti-microbial activity of Methyl Salicylate against *staphylococcus aureus*

Table 4

Test organism's	Zone of inhibition (mm) (0.1%)	Minimum inhibitory concentration(µg/ml) (0.02%)
Staphylococcus aureus	21.8±1.2	75±1.5
For standard	14.8±0.9	125±0.9

Fig. 6: Inhibition zone increased by Methyl salicylate against *staphylococcus aureus* (gram- positive bacteria).

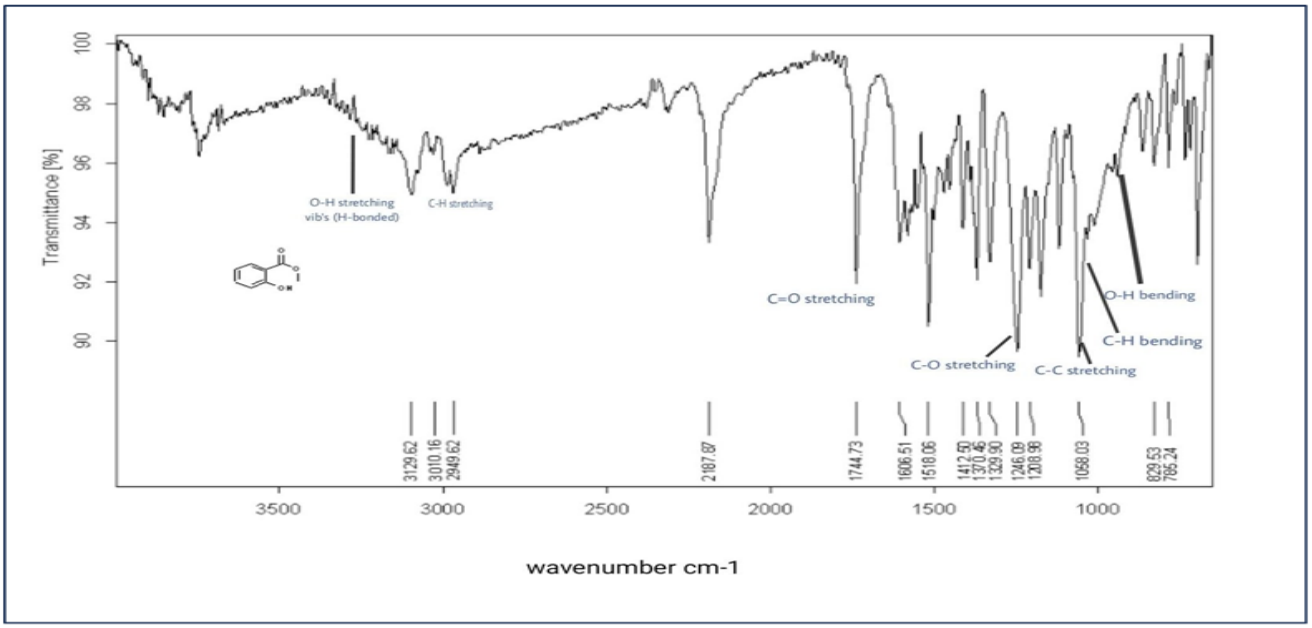
6. Anti-fungal activity of Methyl Salicylate against *candida albicans*

Table 5

Test organisms	zone of inhibition (mm) (0.1%)	Minimum inhibitory concentration (µg/ml) (0.02%)
Candida albicans	20.0±0.5	125±1.0
For standard	25.0±1.0	75±1.5

Fig. 7: Inhibition zone increased by Methyl Salicylate against *candida albicans* (gram-positive bacteria).

7. Infrared spectral analysis of Methyl Salicylate



The infrared (IR) spectrum graph illustrates the transmittance percentage as a function of wavenumber (cm^{-1}) for a specific compound, depicted in the inset structure. The transmittance axis ranges from 90% to 100%, indicating the proportion of light transmitted through the sample at each wavenumber. Several key absorption peaks are identified on the graph, corresponding to various vibrational modes of the molecule.

Notably, there is an O-H stretching vibration (hydrogen-bonded) peak around 3129.62 cm^{-1}, indicative of hydroxyl groups. The C-H stretching vibrations are observed between 3010.16 and 2949.62 cm^{-1}. A prominent peak at approximately 1744.73 cm^{-1} is attributed to C=O stretching, signifying the presence of carbonyl groups. Additionally, C-O stretching vibrations are noted around 1208.89 cm^{-1} and 1065.03 cm^{-1} while O-H bending occurs near 1410.46 cm^{-1}. The spectrum also shows C-H bending at approximately 1248.09 cm^{-1} and C-C stretching vibrations at around 829.53 cm^{-1} and 786.24 cm^{-1}.

These peaks collectively provide insights into the functional groups present in the compound, including hydroxyl, carbonyl, and possible aromatic C-H and C-C bonds. This detailed IR spectrum analysis is crucial for confirming the molecular structure and understanding the chemical properties of the compound under investigation.

DISCUSSION

The innovative microwave-assisted green synthesis of Methyl Salicylate from birch bark powder represents a significant advancement in the pursuit of sustainable production methods. This approach produces a high-purity product without the reliance on harsh chemicals or excessive energy, thereby demonstrating remarkable efficiency. Moreover, the resulting methyl salicylate exhibits potent antimicrobial properties against Staphylococcus aureus, positioning it as a promising natural agent for pharmaceutical and personal care applications. Furthermore, its excellent solubility in various solvents underscores its versatility, making it an attractive candidate for diverse formulations. This breakthrough underscores the immense potential of green synthesis methods in leveraging renewable resources like birch bark powder, thereby paving the way for future research into sustainable and efficient production routes for valuable compounds.

CONCLUSION

Table 6

PROPERTIES	Conventional method (methyl salicylate)	Green synthesis (methyl salicylate)
Melting point	340-350°c (642-662°c)	150-161°c (318-322°c)
Time	1 hour	5 minutes
Reagents	1. Salicylic acid 2. Methanol 3. Conc.H_2SO_4	1. Extracted salicylic acid 2. Methanol 3. ZnO
Solvents	1. Methanol 2. Methylene chloride	1. Methanol 2. Water
Energy	Heat	Microwave
Yield	92.1%	95%

In recent years, green synthesis approaches have completely revolutionized the production of Methyl salicylate, offering a stark contrast to traditional methods. This innovative approach completes the reaction in just 5 minutes at room temperature, yielding an impressive 95% of the product. It not only reduces energy consumption but also eliminates the need for hazardous substances, making it environmentally friendly and sustainable. Embracing green synthesis can significantly minimize the ecological footprint of the chemical industry and pave the way for a more sustainable future. This breakthrough marks a significant stride forward in the pursuit of sustainable chemical production, with considerable benefits for both industry and the environment.

List of Abbreviations IR- Infrared (Spectroscopy) pH- Power of hydrogen.

REFERENCES

1. Anastas, Paul, and Nicolas Eghbali. "Green chemistry: principles and practice." Chemical Society Reviews, 2010; 39(1): 301-312.
2. Haswell, Stephen J., and Paul Watts. "Green chemistry: synthesis in micro reactors." Green Chemistry, 2003; 5(2): 240-249.
3. Grewal, Ajmer Singh, Karunesh Kumar, Sonika Redhu, and Shashikant Bhardwaj. "Microwave assisted synthesis: a green chemistry approach." International Research Journal of Pharmaceutical and Applied Sciences, 2013; 3(5): 278-285.
4. Kaur, Parminder, and Anshul Chawla. "Green synthesis, structural characterization and pharmacological evaluation for analgesic and anti-inflammatory activities of salicylic acid based triazolothiadiazole derivatives." Eur J Biomed Pharm Sci., 2018; 5: 472-479.

5. Özokan, Gökhan, Derya Cansız, Abdulkerim Bilginer, İsmail Ünal, Merih Beler, A. Ata Alturfan, and Ebru Emekli-Alturfan. "Synthesis of salicylic acid from wintergreen oil by green chemistry overcomes its cytotoxicity in keratinocyte cells and teratogenicity in zebrafish embryos." Toxicology Mechanisms and Methods, 2024; 34(2): 203-213.
6. Teimouri, Abbas, Alireza Najafi Chermahini, and M. Hassan Ghorbani. "The green synthesis of new azo dyes derived from salicylic acid derivatives catalyzed via baker's yeast and solid acid catalysis." Chemija, 2013; 24(1): 59-66.
7. Yu, Pengxin, Guangyu Sun, Lu Xiong, Boying Zheng, Teng Li, Jun Jiang, Yantao Wang, and Weiran Yang. "Biomass to drugs: Green production of salicylic acid from 2-furoic acid in two steps." Molecular Catalysis, 2022; 521: 112187.
8. Tang, Wei-Renn, Tsunghsueh Wu, and Yang-Wei Lin. "Salicylic acid-sensitised titanium dioxide for photocatalytic degradation of fast green FCF under visible light irradiation." Micro & Nano Letters, 2019; 14(4): 359-362.
9. Ekinci, Deniz, Murat Şentürk, and Ömer İrfan Küfrevioğlu. "Salicylic acid derivatives: synthesis, features and usage as therapeutic tools." Expert opinion on therapeutic patents, 2011; 21(12): 1831-1841.
10. Molleti, Jayaram, and Ganapati D. Yadav. "Green synthesis of methyl salicylate using novel sulfated iron oxide–zirconia catalyst." Clean Technologies and Environmental Policy, 2019; 21: 533-545.
11. Smith, Jacob E. Lee. "Synthesis of Methyl Salicylate."
12. Mao, Ping, Zizhen Liu, Meng Xie, Rui Jiang, Weirui Liu, Xiaohong Wang, Shen Meng, and Gaimei She. "Naturally occurring methyl salicylate glycosides." Mini reviews in medicinal chemistry, 2014; 14(1): 56-63.
13. Ojha, Pawan Kumar, Darbin Kumar Poudel, Sabita Dangol, Anil Rokaya, Sujan Timsina, Prabodh Satyal, and William N. Setzer. "Volatile constituent analysis of wintergreen essential oil and comparison with synthetic methyl salicylate for authentication." Plants, 2022; 11(8): 1090.
14. Kuriakose, G., and N. Nagaraju. "Selective synthesis of phenyl salicylate (salol) by esterification reaction over solid acid catalysts." Journal of Molecular Catalysis A: Chemical, 2004; 223(1-2): 155-159.
15. Taşdemir, Harun, Semih Traş, Yesim Çat, Sonay Gürer, and Akın Sağırlı. "Zinc-mediated efficient and environmentally benign synthesis of salicylate esters." Flavour and Fragrance Journal (2024).
16. Ahmed, Shakeel, Mudasir Ahmad, Babu Lal Swami, and Saiqa Ikram. "Green synthesis of silver nanoparticles using Azadirachta indica aqueous leaf extract." Journal of radiation research and applied sciences, 2016; 9(1): 1-7.
17. Sangeetha, Gunalan, Sivaraj Rajeshwari, and Rajendran Venckatesh. "Green synthesis of zinc oxide nanoparticles by aloe barbadensis miller leaf extract: Structure and optical properties." Materials Research Bulletin, 2011; 46(12): 2560-2566.
18. Elumalai, K., and Sivasangari Velmurugan. "Green synthesis, characterization and antimicrobial activities of zinc oxide nanoparticles from the leaf extract of Azadirachta indica (L.)." Applied Surface Science, 2015; 345: 329-336.
19. Sun, Qian, Xiang Cai, Jiangwei Li, Min Zheng, Zuliang Chen, and Chang-Ping Yu. "Green synthesis of silver nanoparticles using tea leaf extract and evaluation of their stability and antibacterial activity." Colloids and surfaces A: Physicochemical and Engineering aspects, 2014; 444: 226-231.
20. Carmona, Erico R. Noelia Benito, Tanya Plaza, and Gonzalo Recio-Sánchez. "Green synthesis of silver nanoparticles by using leaf extracts from the endemic Buddleja globosa hope." Green Chemistry Letters and Reviews, 2017; 10(4): 250-256.