Synthesis and Nematicidal Activity of Mannich Bases of Kojic Acid

Yousra Naeem[1]*, Lubna Abidi[1], Shaheen Faizi[2], Erum Iqbal[3]

[1]Department of Chemistry, Jinnah University for Women, 5-C Nazimabad, Karachi-74600 Pakistan.

[2]H.E.J. Research Institute of Chemistry, International Center for Chemical and Biological Sciences, University of Karachi, Karachi-75270, Pakistan.

[3]National Nematological Research Center (NNRC), University of Karachi, Karachi-75270, Pakistan.

*E-mail: yousranaeem84@yahoo.com

ABSTRACT

Root knot nematodes, which are extensively distributed throughout the world, are essential plant parasites that live in plant roots and combine with other plant pathogens to create disease complexes. In order to control plant parasitic nematodes, different nematicides are used. Nematicides effectively control nematode, but their use has environmental and safety concerns. The concerns about their environmental and safety impacts have led to increased scrutiny and the development of more sustainable nematode management practices in agriculture. Kojic acid (KA), a bioprivileged-pyrone, is a naturally occurring metabolite which has great importance in the field of medicines, cosmetics and pharmaceutical industry. It is also used in agriculture as a pesticide, insecticide and nematicide and acts as a plant growth regulating agent. Mannich reaction is a versatile multicomponent reaction (MCR) which has great utility in the synthesis of natural products and pharmaceuticals. These reactions have been employed in various synthetic transformations in order to reduce many steps which are usually involved in classical methods.

The current study is focused to overcome this problem. In this regard Mannich bases of kojic acid were formed with aromatic aldehydes and substituted anilines which afforded two new Mannich bases in fair yields. The structures of these products were elucidated through spectral studies. Besides, the nematicidal activity of these products was also determined against root-knot nematode *Meloidogyne javanica* which showed promising results.

Keywords: Kojic Acid, Multicomponent Reactions, Mannich Reaction, Nematicidal Activity.

INTRODUCTION

Plant-parasitic nematodes (PPNs) lead to substantial economic losses, especially *Meloidogyne spp*. being the most detrimental to numerous crops globally. They have a direct impact on agricultural production by damaging plant root systems, which reduces fruit and crop yields. *Meloidogyne javanica*, a tropical root-knot nematode (RKN) that poses a significant agricultural threat affects more than 770 plant species, including tea, grapes, vegetables, fruit trees, grains, and ornamentals. This nematode result in direct damage by producing galls (root knots), abnormal swellings in the root system that impair nutrient and water intake, resulting in stunted growth, wilting, and considerable yield losses. *M. javanica* exacerbates plant diseases by interacting with soil-borne pathogens such *Thielaviopsis*, *Fusarium*, *Phytophthora*, and *Ralstonia solanacearum*. This combination causes complex disease syndromes and significant agricultural losses, emphasizing the critical need for an effective management strategy. Due to the negative impact of RKNs on agriculture, research has turned from chemically hazardous nematicides to safer, environmentally acceptable alternatives (Zaidi *et al*., 2025).

Kojic acid (KA), a weak acid-pyrone is produced by species of fungi and also from different plants. KA is a versatile synthon used in MCR for the preparation of various biologically active compounds. It is widely used as cosmetic agent, tyrosinase inhibitor, antimicrobial, cytotoxic, antibiotic, antispeck and radio protective

agents, a food additive and flavor enhancer as well as an insecticide, pesticide and nematicides in agriculture (Bhardwaj *et al*., 2025).

Mannich reaction, a well-known MCR, is a condensation reaction of three components *i.e.,* active hydrogen, primary or secondary amine and aldehyde which gives □-amino ketones commonly known as Mannich bases. These bases play an important role in the synthesis of biologically active lead compounds such as anticancer, antibiotic, antimalarial, analgesic, antiviral, anticonvulsant, anti-inflammatory activities *etc.* (Rodriguez *et al.*, 2025).

As part of our continuous efforts to discover safe and cost-effective nematicidal agents, the current work is focused on the preparation of Mannich bases of kojic acid with aldehyde and anilines and the determination of their nematicidal efficacy against root-knot nematode *M. javanica* larvae. These bases have emerged as a potent nematicidal agent and can be used as an alternative remedy in agriculture problems.

OBJECTIVE

The aim of the current research is to prepare Mannich bases of kojic acid in one step by using different aromatic amines with aromatic aldehydes in different reaction conditions and determination of the bioactivity profile and the nematicidal activity of KA of these derivatives in order to obtain safe, cheap and effective drugs and nematicidal agents (especially for agriculture).

METHODOLOGY

This research is a qualitative and quantitative approach to design novel Mannich bases of bioprivileged kojic acid (KA) with aromatic aldehydes and anilines.The products were synthesized at room temperature without any catalyst in green environmentand purified, their yields were determined and their structures were analyzed and confirmed through different spectral studies such as NMR, EIMS, UV and IR techniques. The nematicidal activity of these pure products were determined against root-knot nematode*Meloidogyne javanica*larvaeand compared with the standard.

KEY FINDINGS

In present studies, two new Mannich bases of kojic acid (1 and 2) were synthesized. Both of these Mannich bases showed potent nematicidal activity against the larvae of root-knot nematode *Meloidogyne javanica* when compared with the standard.

CONCLUSION

Mannich reactions of kojic acid (KA) were performed by using different benzaldehydes and anilines which afforded two new Mannich bases 1 and 2 which were emerged as potent nematicidal agents when tested against root-knot nematode *Meloidogyne javanica* larvae.

This simple approach will be used in future to produce unique, large and novel library of Mannich bases of KA in green environment with economic significance. The other biological activities such as anticancer, anti-inflammatory, antimicrobial activities etc.and other applications of these bases will also be determined in order to evolve in to useful products.

REFERENCES

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