PREFACE

The Thesis entitled **Shikonin: Comparative Study of Signaling Pathways in Multiple Therapeutic Areas** encompasses the research work carried out in Department of Bio & Nano Technology, Guru Jambheshwar University of Science & Technology, Hisar, Haryana and Molecular Pharmacology Laboratories in the Department of Biology, TCG Life Sciences, Kolkata for the degree of Doctor of Philosophy in Biotechnology.

The use of various herbal remedies and preparations are described throughout human history representing the origin of modern medicine. Many conventional drugs originate from plant sources: some of the most effective drugs are plant based, such as Aspirin derived from bark of willow, Digoxin derived from foxglove, Quinine derived from the bark of cinchona, and Morphine derived from the opium poppy. The development of drugs from plants by drug companies encourages large scale pharmacological screening of herbs.

Shikonin ($C_{16}H_{16}O_5$) is a red naphthoquinone substance, found in the roots of plants that belong to family Boraginaceae like *Arnebia hispidissima*, *Arnebia euchroma*, *Lithospermum erythrorhizon* and *Onosma paniculatum*. It is a natural medicinal substance with a wide spectrum of pharmacological activities. In last few decades, there has been significant increase in research activity on shikonin to explore its mechanism and cellular signaling pathways in multiple disease areas. Shikonin has been extensively investigated for its anticancerous property. Over the years, its effects in many other therapeutic areas are also reported, but target specific effect of shikonin is largely unknown. Since shikonin is a proven medicinal substance with diverse pharmacology and has not been characterized completely for its precise mechanism of action, there remains a huge need to explore shikonin in terms of its specific and targeted cellular signaling in each disease area along with its *in vivo* efficacy.

The present study has been carried out with best effort to explore the unrevealed targeted effect of shikonin on disease relevant novel targets in diverse therapeutic area. The endeavor not only includes pharmacological screening but also invades to the animal level

to throw insight on the underlying mechanism of action and translation of *in vitro* efficacy to *in vivo* efficacy.

The Thesis consists of six chapters. It begins with short Introduction in Chapter 1, presenting the biosynthesis, pharmacokinetic properties and pharmacology of shikonin. At the end, the chapter lists the major aims and purposes of the study. Chapter 2 is Review of Literature, which recapitulates the various studies on therapeutic potential of shikonin. Chapter 3 deals with Materials and Methods. It is an experimental gateway which describes the various research designs and techniques used in this study. Chapter 4 describes the Results, which deals with the analysis of data in tabulated and figure formats. The outcome of the results in connection with comparative studies has been discussed in Chapter 5. Chapter 6 is of Summary and Conclusions, devoted to the analysis of results and the advancement of knowledge by this study in comparison with published work.

In this research, we focused on target specific effect of shikonin in multiple therapeutic areas and demonstrated that activity of shikonin mediates via specific disease relevant targets. Our study demonstrates the anti nociceptive property of shikonin in pain pharmacology. This study showed significant analgesic effect of shikonin in various animal pain models probably via sodium channel modulation. Our results also reveal the anti-inflammatory, anti-cancerous and anti-diabetic properties of shikonin.

All findings captured in this thesis provide powerful rationale for the development of shikonin as a candidate medicine. In summary therapeutic intervention by shikonin through several physiological targets including GPCRs, ion channels, proteins and enzymes may provide novel strategies for the development of effective treatment against various diseases.

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