Summary
A brief description of all chapters of the thesis entitled “Synthesis and biological activity evaluation of cyclohexane-1,2-diamine, metronidazole, curcumin and thymol derivatives” is described here.

This thesis has been divided into four chapters:

**Chapter 1:** Synthesis, Antimicrobial Activity and Cytotoxicity Evaluation of Unsymmetrical and Symmetrical Cyclohexane-1,2-diamine Derivatives

**Chapter 2:** Synthesis and Biological Activity Evaluation of Metronidazole Based Compounds

**Chapter 3:** Synthesis and Anticancer Activity Evaluation of Curcumin Analogues

**Chapter 4:** Synthesis and Antituberculosis Activity of Thymol Based Schiff Bases and Triazoles

**Chapter 1: Synthesis, Antimicrobial Activity and Cytotoxicity Evaluation of Unsymmetrical and Symmetrical Cyclohexane-1,2-diamine Derivatives**

Cyclohexane moiety has always played a unique role in the organic chemistry and a large number of compounds such as bromhexine, ambroxol and oxaliplatin, having cyclohexane motif have been developed as a drug molecule. In this chapter total 99 cyclohexane-1,2-diamine derivatives were synthesized which includes unsymmetrical cyclohexane-1,2-diamines, analogues of SQ109 (a phase II clinical trial candidate for TB) and symmetrical cyclohexane-1,2-diamines (with long alkyl chain, heterocyclic ring and alkoxy substituents). Most of the compounds were found to be highly active with MIC 0.008-1.0 µg/mL against Gram-positive (S. aureus and S. epidermidis) and Gram-negative (E. coli and P. aeruginosa) bacterial strains. The unsymmetrical compounds when screened against M. tuberculosis exhibited significant activity with MIC value in the range 3.125-50 µM. While the SQ109 analogues and symmetrical cyclohexane-1,2-diamine derivatives exhibited MIC 7.6-20 µM against
H37Rv. Some compounds were screened against Hela cell line for their cytotoxicity evaluation. The most active compounds were found to be non-hemolytic at concentration higher than their MIC value. Methicillin resistant *S. aureus* was incubated with these compounds and SEM experiments showed pronounced effect of these compounds on membrane morphology of the bacterial cells.

Figure I: Cyclohexane-1,2-diamine derivatives
Chapter 2: Synthesis and Biological Activity Evaluation of Metronidazole Based Compounds

Metronidazole (MTZ) has been used for the treatment of infectious diseases caused by bacteria and protozoa. Total 138 hybrid molecules containing metronidazole and other biologically active pharmacophores such as triazole, styrene and thiazolidinone were synthesized in this chapter.

Some of the synthesized metronidazole derivatives were tested for their in vitro biological activity. The metronidazole-triazoles showed a good level of activity against S. aureus, S. epidermidis, E. coli and P. aeruginosa bacterial strains with IC$_{50}$ ranging between 0.003-0.670 µg/mL. The MIC values of these compounds were found to be 0.0084-92.3600 µM against E. histolytica. But, the MTZ-triazole hybrids were found to
be inactive against *M. tb* H37Rv at 50 µg/mL concentration. Few of the MTZ-styryl hybrids when screened against Hela cell line were found to be cytotoxic at high concentration (50 µM).

**Chapter 3: Synthesis and Anticancer Activity Evaluation of Curcumin Analogues**

Curcumin the active constituent of turmeric is used for the treatment of cancer (leukemia, colon, liver, breast and prostate), Alzheimer’s disease, HIV, chronic inflammations, oxidative stress and cystic fibrosis. Curcumin exhibits anti-inflammatory, anti-oxidant, anti-viral and anti-angiogenic properties. It also causes hypocholesterolemic effects in diabetic patients.

![Curcuminoids under present study](image_url)

In this chapter total 72 compounds were synthesized which include 1,3-diketone curcumin (C-7) analogues, monoketone curcumin (C-5) ether and oxazine analogues. Some of the synthesized compounds were screened against Hela cell line and were found to be cytotoxic at very high concentration.
Chapter 4: Synthesis and Antituberculosis Activity of Thymol Based Schiff Bases and Triazoles

Thymol is a naturally occurring monoterpene phenol and shows antibacterial, antifungal, antitumor and anti-inflammatory activities. It is also acts as an antioxidant, free radical scavenger and antilipid peroxidative agent.

![Diagram of Thymol Schiff bases and triazoles](image)

Figure IV: Thymol Schiff bases and triazoles

In this chapter total 62 compounds which include thymol-Schiff bases and thymol-triazole hybrids were synthesized. The thymol-Schiff's bases synthesized were found to be moderate to weakly active against *M. tb* H37Rv *in vitro* (MIC = 6-20 µg/mL). While the thymol-triazoles exhibited weak activity against *M. tb*. 
**Publications**


**Oral Presentation**

1. Talk titled as “*Synthesis of cyclohexane diamine derivatives as antimicrobial agents.*” Presented at the 7th Junior National Organic Symposium Trust (J-NOST) Conference for research scholars at IISER Mohali, India, on dated 15th-18th Dec, 2011.

**Poster Presentations**

1. Presented a poster titled as “*Synthetic library of cyclohexane-diamine derivatives as potential antimicrobial agents*” in the 16th ISCBC-International Conference at Solapur, India on dated 21st-24th Jan, 2012.

3. Presented a poster titled as “Cyclohexane-1,2-diamine derivatives: Synthesis and antimicrobial activity evaluation” in the 15\textsuperscript{th} ISCB International Conference (Commemorating 2011 as the international year of chemistry) at Rajkot, Gujrat, India, on dated 4\textsuperscript{th}-7\textsuperscript{th} Feb, 2011.

4. Presented a poster titled as “Synthesis of benzyl-[3-(benzylamino-methyl)-cyclohexylmethyl]-amine derivatives and metronidazole–triazole conjugates and their antibacterial activity evaluation” in the 4\textsuperscript{th} Indo-Italian Seminar on Green Chemistry and Natural Products, at Department of Chemistry, University of Delhi, India, on dated 17\textsuperscript{th} Nov, 2010.

5. Presented a poster titled as “Synthesis and antibacterial activity evaluation of metronidazole–triazole conjugates and benzyl[3-(benzylamino-methyl)-cyclohexylmethyl]-amine derivatives” in the National Conference on Green and Sustainable Chemistry, at BITS-Pilani, India, on dated February 19\textsuperscript{th}-21\textsuperscript{st}, 2010.

6. Presented a poster titled as “Metronidazole-triazole conjugates as antibacterial and antiamoebic agents” in the 14\textsuperscript{th} ISCB International Conference, Chemical Biology for Discovery: Perspective and Challenges, at CDRI-Lucknow, on dated 15\textsuperscript{th}-18\textsuperscript{th} January, 2010.