CONCLUSIONS:

In the present investigation, five series of mono-substituted-(179, 186, 193, 200 and 206) and di-substituted-2,3,3a,4,5,6-hexahydropyrazoles (180-184, 187-191, 194-198, 201-205 and 208-212) were synthesized, characterized and evaluated for their anti-cancer and antimicrobial studies. The results of the studies can be summarized as follows:

A. The hexahydropyrazoles were synthesized in appreciable yield. The spectroanalytical data (UV, IR, ^1^H-NMR, MS and C, H, N) of synthesized compounds were found in agreement with the assigned molecular structure.

B. The synthesized compounds were evaluated for their anti-cancer (MTS assay on cancer-cell lines, Tubulin Binding Assays) and antimicrobial (antibacterial and antifungal) activities. The observations from these studies can be explained as follows:

B.1. Evaluation of anti-cancer activity

B.1.i. MTS assay on cancer-cell lines:

The presence of hexahydropyrazole moiety has yielded active compounds with an antiproliferative activity in all the five cell lines tested. The most active compounds from for anti-cancer activity as evidenced by their GI_{50} values:

- “3-(4-Methoxyphenyl)-2-(methylsulfonyl)-2,3,3a,4,5,6-hexahydrocyclopenta[c]pyrazole” (189)
- “3-(4-Fluorophenyl)-2,3,3a,4,5,6-hexahydro-2-tosylcyclopenta[c]pyrazole” (181)
- “3-(4-Fluorophenyl)-2-(methylsulfonyl)-2,3,3a,4,5,6-hexahydrocyclopenta[c]pyrazole” (182)

B.1.ii. Tubulin binding assay:

The most active compounds (MTS assay) have shown binding to tubulin with good affinity as evidenced by their K_{D} values:
• “3-(4-Methoxyphenyl)-2-(methylsulfonyl)-2,3,3a,4,5,6-hexahydrocyclopenta[c]pyrazole” (189)

• “3-(4-Fluorophenyl)-2-(methylsulfonyl)-2,3,3a,4,5,6-hexahydrocyclopenta[c]pyrazole” (182)

The two independent experiments i.e. MTS assay and tubulin binding assay have shown similarity in results, as the most active compound 189 binds to tubulin with highest affinity.

B.2 Antimicrobial activity

B.2.i. Evaluation of Antibacterial Activity:

The results of antimicrobial studies by ELISA plate method indicated that the following compounds were the most active compounds for antibacterial activity as evidenced by their pMIC values:

• “3-(4-Fluorophenyl)-2-[(4-chlorophenyl)sulfonyl]-2,3,3a,4,5,6-hexahydrocyclopenta[c]-pyrazole” (183)

• “3-(4-Methoxyphenyl)-2-[(4-nitrophenyl)sulfonyl]-2,3,3a,4,5,6-hexahydrocyclopenta[c]-pyrazole” (187)

• “3-(4-Chlorophenyl)-2-[(4-nitrophenyl)sulfonyl]-2,3,3a,4,5,6-hexahydrocyclopenta[c]-pyrazole” (201)

• “3-(4-Chlorophenyl)-2-[(4-chlorophenyl)sulfonyl]-2,3,3a,4,5,6hexahydrocyclopenta[c]-pyrazole” (204)

B.2.i. Evaluation of Antifungal Activity:

The following compounds were the most active compounds for antifungal activity as evidenced by their pMIC values:

• “3-(4-Fluorophenyl)-2-[(4-nitrophenyl)sulfonyl]-2,3,3a,4,5,6-hexahydrocyclopenta[c]-pyrazole” (180)
C. QSAR studies:

2D-QSAR studies were carried out to find out the correlation between the physicochemical characteristics of the synthesized hexahydropyrazoles and their antimicrobial activity studies. The following descriptors contribute to the respective antimicrobial activities of compounds:

- **S.aureus**: SAMostHydrophobic, HydrophilicDistance, DipoleMoment, SkHydrophilicArea, SsCH3E-index, Quadrupole2.
- **B.Subtilis**: Chi3Cluster, SsClcount, Chi2, SaasCcount, Chi2, CchiV5chain, Chi4pathCluster, ChlorinesCount.
- **E.Coli**: SsssNcount, SsCH3E-index, RotatableBondCount, SdssCE-index, SsCH3E-index, SssOE-index, SsssNcount, SsFE-index.
- **P. areuginosa**: SsCH3count, H-DonorCount, SsFcount, AlphaR, T_C_F_2.
- **C.albicans**: T_2_Cl_6, SssCH2E-index, SdsNE-index, SaasCcount, SdssCE-index, SdsNE-index, Slogp, SssOE-index.
- **A.niger**: T_S_Cl_7, K2alpha, SaaCHcount, Chi6chain, SsOHE-index, chiV3Cluster, SsssNHE-index, FluorinesCount, SdOE-index.

“The generated models include clearly-defined physiochemical descriptors and these may be utilized in future studies for the analysis of large number of compounds and computational screening of molecular databases for modeling antimicrobial activity of new derivatives of 2,3,3a,4,5,6-hexahydrocyclopenta[c]pyrazoles. These will also offer clues for structural modifications that can improve the activity.”
**Future Plan:**

In our study, the following compounds have been found to be most active for the following activities:

- **181, 182 and 189** (Anticancer activity)
- **183, 187, 201 and 204** (Antibacterial activity)
- **180, 188, 194 and 201** (Antifungal activity)

These compounds may be screened further for their detailed computational, pharmacological, toxicological and clinical studies.