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# SYNTHESIS, ANTI MICROBIAL ACTIVITY AND DOCKING STUDY OF SALICYLANIDES

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## ABSTRACT

Discovery of new efficient antibiotics is very challenging task. Due to increasing resistance power of bacteria, fungi and viruses against many antibiotics; searching of effective antibiotic is more difficult job. Salicylanides were synthesized and evaluated for their antimicrobial activity in vitro. All the compounds are characterized by spectroscopic techniques such as FTIR, $H^1$ NMR, $C^{13}$ NMR and Mass. Molecular docking of these compounds is carried out in silico. Molecular docking of these compounds is done with β-Ketoacyl-acyl carrier protein synthase III from Escherichia coli (ecKAS III pdb id: 1HNJ) as a receptor responsible for growth of bacteria. The results show that all Salicylanides are excellent inhibitors of β-Ketoacyl-acyl carrier protein synthase III.

**KEYWORDS:** Salicylanides, Molecular docking, antimicrobial activity, protein etc.

## INTRODUCTION

In recent days the spread of fungal, viral and bacterial diseases affect the health of humans and their livestock adversely. To cure these diseases generally antibiotics are used but the frequent use of some antibiotics; their antibiotics resistance enhances that leads the subjugation of antibiotics. The lethal disease like tuberculosis causes millions of deaths every year in the world. This disease has been a threat to human race from many centuries. Though modern medicine has made significant advancement in treating this disease, the prolonged treatment leads to negligence that makes the diseases chronic and many a times it causes the death.

Salicylanides are the important class of compounds which show various biological activities such as antimicrobial[1-4,6], herbicidal[4], antifungal[5,6], antimycobacterial[7-12], antioxidant and anticoagulant[13] etc. Salicylanides are also used in dyes, pigment and pharmaceutical industries.[14] They play vital role in rupturing of cell wall so that it inhibits the growth of bacteria. Salicylanides and their derivatives act as an annihilator against broad spectrum of diseases. Salicylanides perform as an extirpator against molluscas, helminthes and viruses.[15] They are analgesic, antipyretic, anti-inflammatory[16, 17, 18], anti-malarial and anti-leishmanial[19] agents. They also possess anticancer[20], anti-staphylococcal[21] properties. Salicylanides and their derivatives are substantial building blocks in medicinal and pharmaceutical chemistry.[22] These derivatives act as vital inhibitors of aryl hydrocarbon receptor (AhR)[23] responsible for cancer. They restrain the growth of HIV-1 integrase protein[24], Cyclooxygense (COX-2[25], tyrosinekinase (PTK)[26], β-ketoacyl-acyl carrier protein synthase III[27], isocitralyse, methionine, aminopeptidase etc. This expunging property of Salicylanides derivates makes it significant constituent of pharmaceutical chemistry. Salicylanides are important precursor and synthetic molecular targets in organic synthesis. They are very effective against the parasite toxoplasma gondii responsible for eye disease and brain disease.[28] This wide range of biological properties of Salicylanides makes them crucial synthetic molecular targets for many researchers.

In the present study, Salicylanides are synthesized using phosphorous trichloride and screened for their antimicrobial activity in vitro. These compounds are exposed to four bacterial strains including two gram positive, two gram negative bacteria and two fungal strains.

Molecular docking was also carried out in silico to gain knowledge about the pharmacological activity of these molecules using the software hex 6.0.[29] In our study for molecular docking, we have taken the enzyme from Escherichia coli β -Ketoacyl-acyl carrier protein synthase III (ecKAS III pdb id: 1HNJ)[27] as a receptor responsible for growth of bacteria and our synthesized derivatives as ligands.

## MATERIALS AND METHODS

### General Method

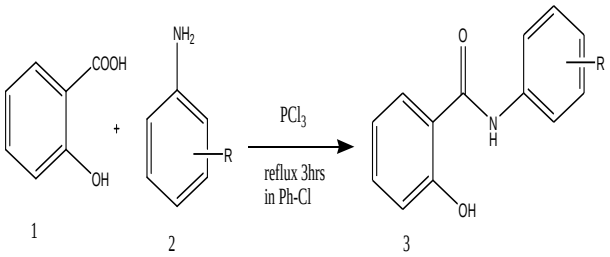
All the reagents and solvents were purchased from Sigma-Aldrich and they were used as received. Melting points were determined using open capillaries method and the reported values are uncorrected. Infrared spectra (ATR) were recorded on FT-IR spectrometer Shimdzhu 8400S FT-IR in the range of 4,000–400cm−1. The NMR spectra were recorded on a 500MHz instrument at ambient temperature using deuterated dimethylsulfoxide (DMSO-*d6*) solutions of the samples. The chemical shifts δ are given in ppm, with respect to tetramethylsilane as an internal standard. The structures of compounds are drawn with the help of chem. draw 8.0. The mass spectra were recorded on 6460 Triple Quadruple LC/MS model.

### Tools and Materials used

For our present study we used bioinformatics tools, biological databases like Drug Bank, PDB (Protein Data Bank) and software's like Hex, Biova discovery studio 4.5visualizer.Chem. draw is used for effective drawings of 2D-3D structures of compounds and it helps the chemists to draw molecules, reactions and schematic diagrams, calculate chemical properties conveniently. The 2D-3D structures of all salicylanides derivatives are constructed on chem. draw 8.0.Then these chem. draw files are converted into protein data bank files using Biova discovery studio 4.5visualizer. We obtained crystal structure of β-Ketoacyl-acyl carrier protein synthase III (pdb id: 1hnj) for antibacterial activity from the Protein Data Bank. All these structures are utilised for molecular docking process using software Hex 6.0.

## RESULTS AND DISCUSSION

Salicylanides can be prepared by using salicylic acid, different primary aromatic amines (anilines) as a starting material, phosphorous trichloride as a reagent and chlorobenzene as a solvent reflux for three hours under conventional conditions (scheme1).




**Scheme1: Synthesis of Salicylanides**

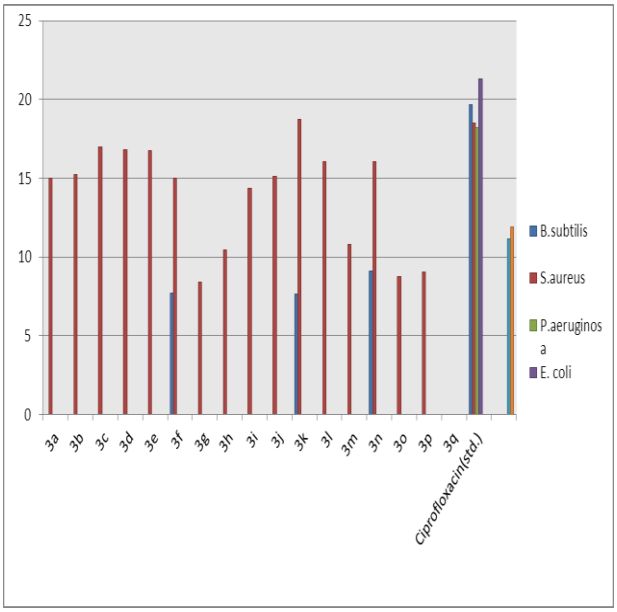
### In vitro Antimicrobial Evaluation

Antimicrobial properties ofseventeen salicylanides were assayed against bacterial strain. This testing is carried out using disc diffusion method. Various bacterial strains - *Staphylococcus aureus* (NCIM 2079), *Bacillus subtilis (*NCIM 2250), *Escherichia coli* (NCIM 2109), *Pseudomonas aeruginosa (*NCIM 2036*)* and fungal strains *Candida albicans* (NCIM 3471), *Aspergillus niger (*NCIM *545)* were used as test microorganism to evaluate the antimicrobial testing of newly synthesized compounds.

Table1overviews the antibacterial and antifungal properties.

**Table1: In vitro antibacterial activity of Salicylanides towards bacteria and fungi**.

| Sr. No | Compound Code | Amines | B. subtilis | S. aureus | P. aeruginosa | E. coli | C. albicans | A. niger |
|---|---|---|---|---|---|---|---|---|
| 1 | 3a | 2-chloroaniline | - | 14.99 | - | - | - | - |
| 2 | 3b | 3-methoxy aniline | - | 15.22 | - | - | - | - |
| 3 | 3c | aniline | - | 16.99 | - | - | - | - |
| 4 | 3d | 3- chloroaniline | - | 16.81 | - | - | - | - |
| 5 | 3e | 4-bromoaniline | - | 16.73 | - | - | - | - |
| 6 | 3f | 4- chloroaniline | 7.7 | 14.99 | - | - | - | - |
| 7 | 3g | p-Toludine | - | 8.42 | - | - | - | - |
| 8 | 3h | 4-aminoazobenzene | - | 10.42 | - | - | - | - |
| 9 | 3i | Naphthyl amine | - | 14.34 | - | - | - | - |
| 10 | 3j | p- phenyl diamine | - | 15.12 | - | - | - | - |
| 11 | 3k | o-phenyl diamine | 7.67 | **18.76** | - | - | - | - |
| 12 | 3l | o-Toludine | - | 16.05 | - | - | - | - |
| 13 | 3m | p-anisidine | - | 10.78 | - | - | - | - |
| 14 | 3n | 4-nitroaniline | **9.11** | 16.03 | - | - | - | - |
| 15 | 3o | 3-nitroaniline | - | 8.77 | - | - | - | - |
| 16 | 3p | 2-nitroaniline | - | 9.03 | - | - | - | - |
| 17 | 3q | o-dianisidine | - | - | - | - | - | - |
| 18 | Ciprofloxacin(std.) | | 19.7 | 18.5 | 18.19 | 21.32 | NA | NA |
| 19 | Amphotericin-B(std.) | | NA | NA | NA | NA | 11.12 | 11.92 |




**Graph 1: Biological activities of Salicylanides**

In case of Salicylanides, all Salicylanides shows significant antibacterial activity against S.aureus in vitro. Some Salicylanides such as 3f, 3k and 3n are also active against B.subtilis. The compounds **3a,3b,3c, 3d, 3e, 3f,3i, 3j, 3k, 3l, and 3n** showed very good antibacterial activityagainst S.aureus and compound **3k** is more potent than the standard drug ciprofloxacin. None of the synthesized compound showed antifungal activity against A. niger and C. albicans.

## MOLECULAR DOCKING

Molecular docking study provides the knowledge about the nature and reactivity of the compounds and this helps to judge the biological activity of compounds using computer softwares. It is the method which helps to understand the binding interaction and orientation of drug molecule with enzyme.[30] Molecular docking is the process which is used to predict the protein-ligand complexes.[31] It plays key role in designing of rational drugs to minimise toxicity and side-effects.

Following parameters were used for the molecular docking process.

- Correlation type – Shape + Electrostatics
- FFT Mode – 3D
- Post Processing–MM Energies
- Grid Dimension – 0.6
- Receptor range – 180
- Ligand Range – 180
- Twist range – 360
- Distance Range – 40

Using all these parameters Salicylanides are docked against with β-Ketoacyl-acyl carrier protein synthase III (ecKAS III).

The three dimensional structure of ecKAS III enzyme formed complex with Salicylanides with good binding site. This study enabled us to predict the interaction and orientation of Salicylanides into β-Ketoacyl-acyl carrier protein synthase III (ecKAS III) active sites.We carried out 10 docking operations for each ligand and selected top score for binding affinity of each ligand-enzyme complex.

**Fig 1: Structure of receptor β-Ketoacyl-acyl carrier protein synthase III (pdb id: 1hnj)**

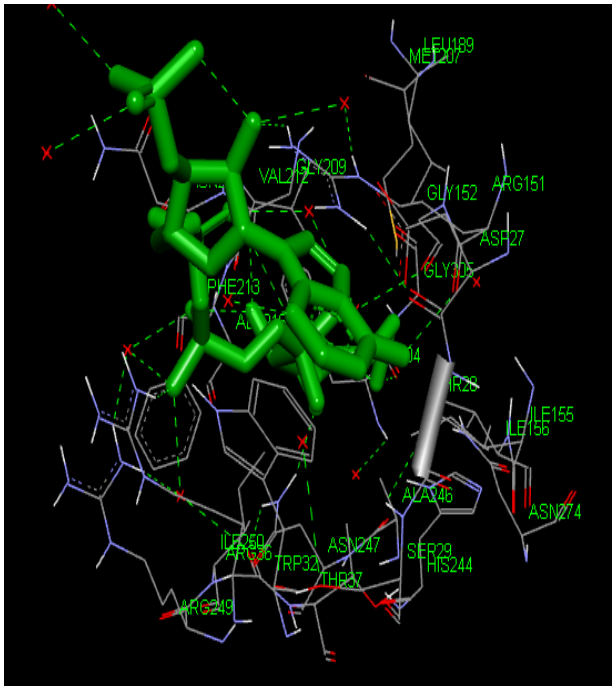



**Fig 2: compound 3c with active site of 1HNJ 2-hydroxy-N-phenylbenzamide**

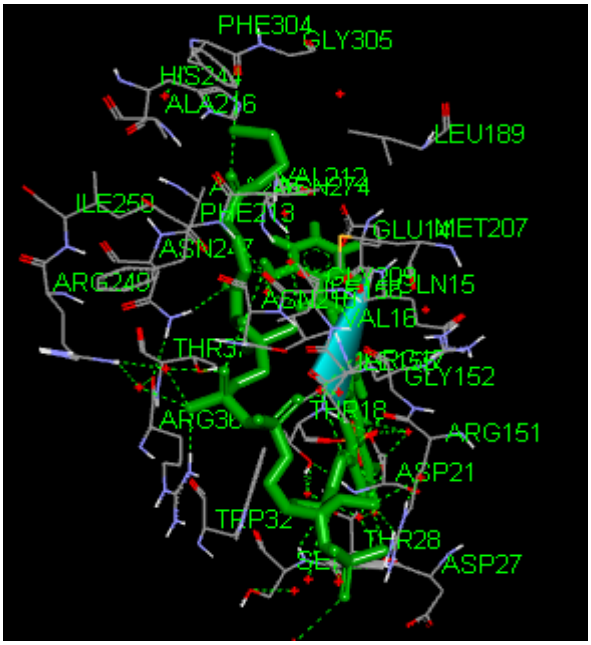



**Fig 3: compound 3j with active site of 1HNJ 2-hydroxy-N-phenylbenzamide**

**Table 2: Binding energies of Salicylanides.**

| Sr. No | Compound Code | E-Value | H Bond |
|---|---|---|---|
| 1 | 3a | -89.11 | 1 |
| 2 | 3b | -86.82 | 1 |
| 3 | 3c | **-1799.76** | 1 |
| 4 | 3d | **-1724** | 1 |
| 5 | 3e | -88.73 | 1 |
| 6 | 3f | -90.13 | 1 |
| 7 | 3g | -71.49 | 1 |
| 8 | 3h | -71.04 | 1 |
| 9 | 3i | -92.7 | 1 |
| 10 | 3j | **-2379.7** | 1 |
| 11 | 3k | -86.24 | 1 |
| 12 | 3l | -104.69 | 1 |
| 13 | 3m | -54.55 | 1 |
| 14 | 3n | -90.58 | 1 |
| 15 | 3o | -58.33 | 1 |
| 16 | 3p | -79.09 | 1 |

We observed that, there are some variation between theoretical and experimental data. In above Salicylanides, compounds **3j, 3c** and **3d** exhibit significant binding interactions with miniumum binding energy. From antibacterial activity and docking study of all these Salicylanides it revealed that compound **3j** is excellent inhibitor of ecKAS III protein ( pdb id: 1HNJ).

## EXPERIMENTAL

### STEP 1: Synthesis of Salicylanides

A suspension of substituted salicylic acid (0.02mol) and a substituted aniline (0.02 mol) in chlorobenzene (100 $cm^3$) was heated under reflux in the presence of $PCl_3$ (0.01 mol) for 3 h. The reaction mixture was filtered while hot, and the product allowed to crystallize upon cooling, which yielded 80-95% of the theoretical amount. The product was recrystallized from ethanol—water.

**1. N-(2-chlorophenyl)-2-hydroxybenzamide (3a)**

Yield: 90%, m.p:170-172$^0$C IR Cm-1:1637.62 (CO amide), 3350 (N-H stretch), 3072.71 (bs,-OH), MS 248.0, $^1$H NMR: 8.3-6.9 (m, 8H), 11.2 (s, 1H, OH), 10. 0(s, 1H, NH), $^{13}$CNMR: 165.91, 158.29, 135.08,133.85,129.4,129.1,127.1,124.9,124.2,122.9, 119.6,117.5 Anal. Calcd. For $C_{13}H_{10}ClNO_2$; C, 63.04; H, 4.07; Cl, 14.31; N, 5.66; O, 12.92. Found; C, 63.0; H, 4.12; Cl, 14.84; N, 5.06; O, 12.01.

**2. 2-hydroxy-N-(3-methoxyphenyl) benzamide (3b)**

Yield: 83%, m.p:145-147$^0$C,IR Cm-1:1597.11 (CO amide), 3329.25 (N-H stretch), 3072.71 (bs,-OH), MS 244.1,$^1$H NMR: 8.0-6.7 (m, 8H), 11.9 (s, 1H, OH), 10.4

(s, 1H, NH), 3.7 (s, 3H),$^{13}$C NMR: 167.19, 160.01, 159.13, 139.86, 134.13, 129.9, 129.5, 119.46,117.75, 113.6, 110.08,107.24,55.46 Anal. Calcd. For $C_{14}H_{13}NO_3$ C, 69.12; H, 5.39; N, 5.76; O, 19.73, Found C, 68.96; H, 5.30; N, 5.26; O, 19.05.

**3. 2-hydroxy-N-phenylbenzamide (3c)**

Yield: 88%, m.p:148-150$^0$C, IR Cm-1:1620.26(CO amide), 3329.25 (N-H stretch), 3072.71 (bs,-OH) MS 213.08, H$^1$NMR; 8.2-6.9 (m, 9H), 11.3 (s, 1H, OH), 10. 0 (s, 1H, NH), $^{13}$C NMR: 165.91,158.29,135.08,133.85,129.4,129.1,127.1,124.9,12 4.2,122.9, 119.6,116.0 Anal. Calcd. For $C_{13}H_{11}NO_2$; C, 73.23; H, 5.20; N, 6.57; O, 15.01 Found; C, 73.05; H, 5.10; O,14.84; N, 6.70.

**4. N-(3-chlorophenyl)-2-hydroxybenzamide (3d)**

Yield: 82%, m.p:188-190$^0$C, IR Cm-1: 1649.19 (CO amide), 3408.33 (N-H stretch), 3130.13 (bs,-OH) MS 248.0,$^1$H NMR: 7.9-6.9 (m, 8H), 11.6 (s, 1H, OH), 10.5 (s, 1H, NH), $^{13}$C NMR: 167.12, 158.70, 140.24, 134.19, 133.56, 130.77,129.67, 124.20,120.71, 119.59, 119.54, 117.68. Anal. Calcd. For $C_{13}H_{10}$ Cl $NO_2$: C, 63.04; H, 4.07; Cl, 14.31; N, 5.66; O, 12.92. Found; C, 62.94; H, 4.12; Cl, 14.35; N, 5.02; O, 12.98.

**5. N-(4-bromophenyl)-2-hydroxybenzamide (3e)**

Yield: 85%, m.p:176-178$^0$C, IR Cm-1: 1612.54 (CO amide), 3306.10 (N-H stretch), 3037 .99 (bs,-OH) MS 292.0, $^1$H NMR:7.9-6.9 (m, 8H), 11.7 (s, 1H, OH), 10.4 (s, 1H, NH), $^{13}$CNMR:167.08,158.85, 138.11, 134.18, 131.99,129.59,123.22,119.51, 118.04,117.70,116.36.
Anal. Calcd. For $C_{13}H_{10}BrNO_2$ C, 53.45; H, 3.45; Br, 27.35; N, 4.79; O, 10.95. Found; C, 53.05; H, 3.41; Br, 27.20; N, 4.81; O, 11.01.

**6. N-(4-chlorophenyl)-2-hydroxybenzamide (3f)**

Yield: 83%, m.p:180-182$^0$C, IR Cm-1: 1649.19 (CO amide), 3408.33 (N-H stretch), 3130.13 (bs,-OH) MS 248.0$^1$H NMR: 8.0-6.9 (m, 8H), 11.7 (s, 1H, OH), 10.6 (s, 1H, NH) $^{13}$C NMR: 167.13, 158.95, 137.66,134.17, 129.56, 129.05,128.31, 122.88, 119.48, 117.94, 117.71. Anal. Calcd. For $C_{13}H_{10}ClNO_2$ C, 63.04; H, 4.07; Cl, 14.31; N, 5.66; O,12.92. Found; C, 62.94; H, 4.12; Cl, 14.35; N, 5.02; O, 12.98.

**7. 2-hydroxy-N-p-tolylbenzamide (3g)**

Yield: 90%, m.p:140-142$^0$CIR Cm-1: 1604.83 (CO amide), 3321.53 (N-H stretch), 3018.70 (bs,-OH) MS 228.1,$^1$H NMR: 7.5-6.9 (m, 8H), 12.0 (s, 1H, OH), 7.9 (s, 1H, NH), 2.37 (s, 3H),$^{13}$C NMR: 168.34, 161.88, 135.26, 134.62, 133.96, 129.73, 125.36, 121.37, 118.95, 118.92, 114.60, 20.96. Anal. Calcd. For $C_{14}H_{13}NO_2$ C, 73.99; H, 5.77; N, 6.16; O, 14.08. Found; C, 73.76; H, 5.89; N, 6.26; O, 14.11.

**8. 2-hydroxy-N-[4-(phenyldiazenyl) phenyl] benzamide (3h)**

Yield: 60%.IR Cm-1: 1591.33 (CO amide), 3315.74 (N-H stretch), 3030.27 (bs,-OH) MS 318.1. H$^1$NMR:8.0-6.9 (m, 13 H), 11.2 (s, 1H, OH), 10.6 (s, 1H, NH), $^{13}$C NMR: 167.13, 158.95,152.7, 148.3, 138.1, 133.6, 131.0, 128.9, 129.1, 129.1,123.2, 123.2, 123.0, 123.0, 121.9, 121.9, 121.5, 119.9, 116.0. Anal. Calcd. For $C_{19}H_{15}N_3O_2$ C, 71.91; H, 4.76; N, 13.24; O, 10.08. Found C, 72.01; H, 5.16; N, 13.50; O, 10.12.

**9. 2-hydroxy-N-(naphthalen-1-yl)benzamide (3i)**

Yield: 60%.m.p:186-188$^0$C IR Cm-1: 1629.90 (CO amide), 3225.09 (N-H stretch), 3063.06 (bs,-OH) MS 264.1, H$^1$NMR: 8.0- 6.9 (m , 11H), 11.0 (s, 1H, OH), 9.6 (s, 1H, NH), $^{13}$C NMR: 167.13, 158.95, 140.8, 133.6, 134.3, 128.9, 128.6, 126.6, 126.0, 125.0, 124.7, 121.5, 121.0, 119.9, 116.0, 109.4. Anal. Calcd. For $C_{17}H_{13}NO_2$ C, 77.55; H, 4.98; N, 5.32; O, 12.15. Found; C, 76.95; H, 5.76; N, 5.22; O, 12.04.

**10. N,N'-1,4-phenylene bis(2-hydroxybenzamide) (3j)**

Yield: 62%.m.p:180$^0$C, IR Cm-1: 1637.62 (CO amide), 3257.88 (N-H stretch), 3057.27 (bs,-OH) MS 349.1 $^1$H NMR: 7.8-6.7 (m, 8H), 11.7 (s, 1H, OH), 9.6 (s, 1H, NH), 2.1 (s, 1H), $^{13}$C NMR: 167.31, 159.54, 135.65, 133.69, 131.84, 130.47, 128.76, 128.67, 126.37, 125.84, 124.96, 119.19, 119.07, 116.34, 18.03. Anal. Calcd. For $C_{20}H_{16}N_2O_4$ C, 68.96; H, 4.63; N, 8.04; O, 18.37. Found; C, 68.16; H, 4.83; N, 9.04; O, 18.40.

**11. N,N'-1,2-phenylene bis (2-hydroxybenzamide) (3k)**

Yield: 63%. m.p:210$^0$C, IR Cm-1:1629.90 (CO amide), 3331.18 (N-H stretch), 3076.56 (bs,-OH) MS 349.1. $^1$H NMR: 7.8-6.7 (m, 8H), 11.7 (s, 1H, OH), 9.6 (s, 1H, NH), 2.1 (s, 1H), $^{13}$C NMR: 167.31, 159.54, 135.65, 133.69, 131.84, 130.47, 128.76, 128.67, 126.37, 125.84, 124.96, 119.19, 119.07, 116.34, 18.03. Anal. Calcd. For $C_{20}H_{16}N_2O_4$ C, 68.96; H, 4.63; N, 8.04; O, 18.37. Found; C, 69.16; H, 4.15; N, 8.14; O, 18.23.

**12. 2-hydroxy-N-o-tolylbenzamide (3l)**

Yield: 75%.m.p:144-146$^0$C, IR Cm-1: 1631.83 (CO amide), 3350.13 (N-H stretch), 3178.79 (bs,-OH), MS 228.1. $^1$H NMR: 8.0-6.9 (m, 8H), 9.1 (s, 1H, OH), 9.6 (s, 1H, NH), 2.35 (s, 3H, $CH_3$), $^{13}$C NMR: 164.8, 160.4, 134.8, 133.6, 134.3, 129.3, 128.9126.0, 124.3, 121.5, 121.5, 124.3, 119.9, 116.0, 15.2. Anal. Calcd. For $C_{14}H_{13}NO_2$; C, 73.99; H, 5.77; N, 6.16; O, 14.08. Found C, 73.90; H, 5.71; N, 6.35; O, 14.11.

**13. 2-hydroxy-N-(4-methoxyphenyl)benzamide (3m)**

Yield: 70%.m.p:225-227$^0$C, IR Cm-1:1612.54 (CO amide), 3406.40 (N-H stretch), 3088.14 (bs,-OH) MS 244.1$^1$H NMR: 8.0-6.7 (m, 8H), 11.9 (s, 1H, OH), 10.4 (s, 1H, NH), 3.7 (s, 3H),$^{13}$C NMR: 167.19, 160.01, 159.13, 139.86, 134.13, 129.9, 129.5, 119.46,117.75, 113.6, 110.08,107.24,55.46 Anal. Calcd. For $C_{14}H_{13}NO_3$ C, 69.12; H, 5.39; N, 5.76; O, 19.73, Found C, 68.96; H, 5.30; N, 5.26; O, 19.05.

**14. 2-hydroxy-N-(4-nitrophenyl)benzamide (3n)**
Yield: 52%.m.p: charred 230$^0$C, IR Cm-1: 1641.48 (CO amide), 3350.08 (N-H stretch), 3064.99 (bs,-OH) MS 259.1. $^1$H NMR: 8.2-6.9 (m, 8H), 11.9 (s, 1H, OH), 10.4 (s, 1H, NH). $^{13}$C NMR: 167.8, 158.95, 144.0, 142.0, 133.6, 128.9, 122.5, 122.5, 121.5, 121.3, 121.3, 119.9, 116.0. Anal. Calcd. For $C_{13}H_{10}N_2O_4$ C, 60.47; H, 3.90; N, 10.85; O, 24.78. Found; C, 60.32; H, 3.80; N, 10.55; O, 24.56.

**15. 2-hydroxy-N-(3-nitrophenyl) benzamide (3o)**
Yield: 47%.m.p: charred 245$^0$C, MS 259.0, IR Cm-1: 1650.48 (CO amide), 3404.47 (N-H stretch), 3020.63 (bs,-OH) MS 259.0. $^1$H NMR: 8.2-6.9 (m, 8H), 11.9 (s, 1H, OH), 10.4 (s, 1H, NH). $^{13}$C NMR: 167.8, 158.95, 144.0, 142.0, 133.6, 128.9, 122.5, 122.5, 121.5, 121.3, 121.3, 119.9, 116.0. Anal. Calcd. For $C_{13}H_{10}N_2O_4$.C, 60.47; H, 3.90; N, 10.85; O, 24.78. Found; C, 60.22; H, 3.52; N, 10.45; O, 24.82.

**16. 2-hydroxy-N-(2-nitrophenyl) benzamide (3p)**
Yield: 55%.m.p:160-162$^0$C, IR Cm-1: 1653.05 (CO amide), 3350.08 (N-H stretch), 3150.20 (bs,-OH) MS 259.1$^1$H NMR: 8.2-6.9 (m, 8H), 11.9 (s, 1H, OH), 10.4 (s, 1H, NH). $^{13}$C NMR: 167.8, 158.95, 144.0, 142.0, 133.6, 128.9, 122.5, 122.5, 121.5, 121.3, 121.3, 119.9, 116.0. Anal. Calcd. For $C_{13}H_{10}N_2O_4$. C, 60.47; H, 3.90; N, 10.85; O, 24.78. Found; C, 60.13; H, 3.82; N, 10.56; O, 24.41.

**17. N, N'-(2,2'dimethoxyphenyl-4,4'diyl) bis(2-hydroxy benzamide) (3q)**
Yield: 71%. IR Cm-1: 1633.15 (CO amide), 3404.47 (N-H stretch), 3020.20 (bs,-OH) MS 485.1. $^1$H NMR: 8.3-6.9 (m, 14H), 10.5 (d, 2H, 2-OH), 9.4 (d, 2H, 2-NH), 3.75 (s, 6H, 2-$OCH_3$), $^{13}$C NMR: 164.8, 164.8, 159.4, 159.4, 153.3, 153.3, 133.6, 133.6, 133.1, 133.1, 128.9, 128.9, 123.1, 123.1, 123.1, 123.1,121.5, 121.5, 120.4, 120.4, 119.9, 119.9, 115.5, 115.5,111.9, 112.5, 55.9, 55.6. Anal. Calcd. For $C_{28}H_{24}N_2O_6$; C, 69.41; H, 4.99; N, 5.78; O, 19.81. Found; C, 65.35; H, 4.96; N, 5.28; O, 20.53.

**18. N-cyclohexyl-2-hydroxybenzamide (3r)**
Yield: 71%. IR Cm-1: 1650.25 (CO amide), 3300.51 (N-H stretch), 3025.22 (b s,-OH) MS 219.13 $^1$H NMR; 8.0-6.9 (m, 4H), 1.96-1.35(m, 10H), 11.2 (s, 1H, OH), 10.4 (s, 1H, NH). $^{13}$C NMR: 167.3, 159.4, 133.6, 128.9, 121.5, 119.9, 116.2, 50.2, 33.8, 33.8, 28.0, 22.9, 22.9. Anal. Calcd. For $C_{13}H_{17}NO_2$ C, 71.21; H, 7.81; N, 6.39; O, 14.59. Found; C, 71.10; H, 8.03; N, 6.56; O, 14.43.

## CONCLUSION

To conclude, eighteen Salicylanides are synthesized successfully. Synthesized compounds are characterized and also checked for the antibacterial and antifungal activity of these ester derivatives in vitro. Among all Salicylanides compound **3k** showed more antibacterial activity against S. aureus as compared to standard drug Ciprofloxacin. Most of the Salicylanides showed very good antibacterial activity. Further Molecular docking of all these compounds is done using β-Ketoacyl-acyl carrier protein synthase III from Escherichia coli (ecKAS III pdb id: 1HNJ) as a receptor responsible for growth of bacteria in silico. All the Salicylanides are good inhibitors of β-Ketoacyl-acyl carrier protein synthase III. Salicylanides, specifically compounds **3c, 3d** and **3j** showed better binding score as compared to their cinnamic acid ester derivatives. Among all the Salicylanides compound **3j** exhibited good binding interactions with β-Ketoacyl-acyl carrier protein synthase III.

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