**Response to Reviewers**

**Reviewer B:**

1) Not all the drugs listed in introduction (fomepizole and sildenafil), are depicted in Fig. 1, so I think it needs to be included?

Ans: Included all the drugs in the Fig. 1

2) In introduction part authors substantiate including of triazole and pyrazole parts in title compounds, but choose of 1-(2,4-dihydroxyphenyl)ethanone (1) core is unclear nether from introduction, nor from discussion part?

Ans: In order to incorporate the triazole and pyrazole scaffolds in the title compounds we have chosen 1-(2,4-dihydroxyphenyl)ethanone (1) core, which has the functional groups to incorporate those required scaffolds.

3) Page 3 “…was carried out by electrophilic substitution reaction of 1-(2,4-dihydroxyphenyl)ethanone (1) …”. Alkylation with alkylhalogenides is a nucleophilic substitution reaction?

Ans: Corrected accordingly.

4) As far as I understand, all compounds 6(a-j) were produced in two different ways with different yields. If it so, there is impossible to say about adopting (“Hence we have adopted the route-1 strategy to synthesize title compounds”) of one of the routes for the synthesis, because both ways were tried for all the compounds. Maybe it is better to say: “route 1 comparing to route 2 is better because of…”?

Ans: Modified accordingly.

5) It is unclear from the text of the article why authors discuss only spectral characteristics of 6g?

Ans: Compound 6g has methyl and methoxy substituents on the core, which could give more scope to explain prominent peaks in HNMR and CNMR spectra.

6) It is incorrect to say about ranges of signal in this case. Appropriate chemical shift must be mentioned. Also it is unclear why authors discuss only β-proton, instead of discussing both α and β?

Ans: Chemical shifts were modified accordingly. α-proton get mixed with aromatic protons and appeared as multiplet.

7) “A broad singlet was observed at δ 13.52 due to OH proton.” This is quite big low field shift for phenolic proton, because in the most cases it is observed at 7-8 ppm. Are there any other comparable data in the literature?

Ans: We have already synthesized and reported few compounds with same OH functionality with that range of chemical shifts.

Ashok, D., Rangu, K., Hanumantha Rao, V. et al. Med Chem Res (2016) 25: 501. doi:10.1007/s00044-016-1505-2.

8) Generally, part dedicated to description of IR, NMR-spectroscopy data is weak and need to be improved or rewritten?

Ans: Modified accordingly.

**Reviewer H:**

1) Status of compounds 7 should be clarified. Are those compounds synthesised in this research, or they are known. Otherwise, corresponding reerences and synthetic and spectral/analytical data should be provided?

Ans: The spectral data of **7a-e** is included in the manuscript and the scanned copies of the 1H NMR and Mass spectra are included in the supporting data.

2) It seems that Cl- or CH3-group are always in para–position in pyrazole aldehyde. Authors should correct that in reaction Scheme?

Ans: Corrected accordingly.

3) Details about LC-MS should be provided, like conditions for HPLC analysis and mode (negative/positive) for spectra recording. In addition, applied ionisation technique must be cited, and writing of mass data should be coordinate with that. Concrete, isotopic patern of halogen derivatives could be visible depending of applied mass spectra conditions?

Ans: Shimadzu LCMS AD conditions:

LC solutions software

PDA-Photo Diod Arrey detector

binary pump

Auto sample Injector

Flow 1 ml/Min

Electron spray Positive mode Ionization - ES+

Solvent condition: Methanol-Water 60-40%

Vaccume 1.00e.004 (Gas cell pirani)

Source temperature : 120 oC

Desolvation Tempefrature : 220 oC

Normal Degasser

Stroke Lenght (ul-micro ltrs) 130

Injection Volume - 3 Micro Ltrs

4) Comparison between traditional and MW procedures for synthesis of derivatives 6 is not adequate, since traditional procedure was performed at room temperature. Even under such mild conditions, yields were ~50%. For appropriate comparison, heating at the same temperature (as in MW) should be applied?

Ans: During optimization study, couple of title compounds were synthesized in heating condition. The yields were either same or unfortunately less compare to room temperature condition. Hence we have compared with room temperature condition.

5)

a) In Discussion, based on data in Table 1, authors concluded that Cu(I) was more successful, and for that reason they choose it for further experiments. Yet, In Scheme 2, authors preserved CuSO4 as optional catalyst for synthesis of derivatives 6 and 7 (route b).

Ans: Inclusion of CuSO4 catalyst in Scheme 2 was an error. Corrected in the Scheme 2.

b) Although CuSO4 was not choosen for further experiments, representative procedures should be given. We sugests termal and MW procedures for entry 3, Table 1?

Ans: Procedures for synthesis of title compounds in presence of CuSO4 catalyst included in the manuscript.

a) Oxidation states of Cu-salts as contributor for reactions outcome should be discused. As well as using of sodium ascorbate with CuSO4?

Ans: Both the cases, the oxidation state of active catalyst involved in the reaction is Cu+1. In CuSO4 condition, sodium ascorbate acts as reducing agent and converts the Cu+2 toCu+1.

6)

a) Coupling constants for all first order coupling signals must be calculated?

Ans: Corrected the spectral data accordingly.

b) Only “complicated” multiplets (m) could be given in the range of chemical shifts. All other signals must be given with single value?

Ans: Modified accordingly.

7) Representative copies of 1H and 13C NMR spectra for derivatives 6a-e and 6f-j (for one of each or more, as authors choose), could be provided, as Supplementary Information data?

Ans: 1H, 13C NMR and Mass spectra of all the derivatives are provided in Supplementary Information.

8) In Abstract: „Compounds 6a, 6d and 6e demonstrated better inhibitory…” Better inhibitory than … Who?

Ans: Corrected the word “better” to “promising”.