

RESULT AND DISCUSSION

❖ *Pyrazolo quinazoline derivatives (KC-1 to KC-10):*

Figure 4.1 [A] shows inhibition against Gram positive bacteria in DMF solutions of all the compounds (KC-1 to KC-10). It is observed that against *Bacillus cereus* (BC), KC-7 exhibited maximum inhibition which is followed by KC-10. KC-2 and KC-8 had no effect against BC. For *Staphylococcus aureus* (SA), maximum inhibition is observed by KC-1 whereas KC-1, KC-5 and KC-8 had no effect. Almost equal effect of compounds KC-3, KC-4, KC-7 and KC-8 are observed against *Corynebacterium rubrum* (CR) and KC-4, KC-9 and KC-10 against *Listeria monocytogenes* (LM). On these two strains, other compounds had no effect at all. Out of these four bacterial strains, LM is most resistant bacteria whereas BC is most susceptible bacteria in DMF.

Figure 4.1 [B] shows inhibition against Gram positive bacteria in DMSO. KC-2 and KC-5 could not inhibit any Gram positive bacteria. KC-1, KC-3, KC-7, KC-8, KC-9 and KC-10 showed moderate inhibition against BC. Only KC-3 and KC-4 could inhibit SA. Compounds KC-1, KC-6, KC-7 and KC-10 showed inhibition against CR whereas KC-3, KC-7 and KC-10 showed inhibition against LM. Thus, in DMSO also, LM is most resistant bacteria whereas BC is most susceptible bacteria in DMF.

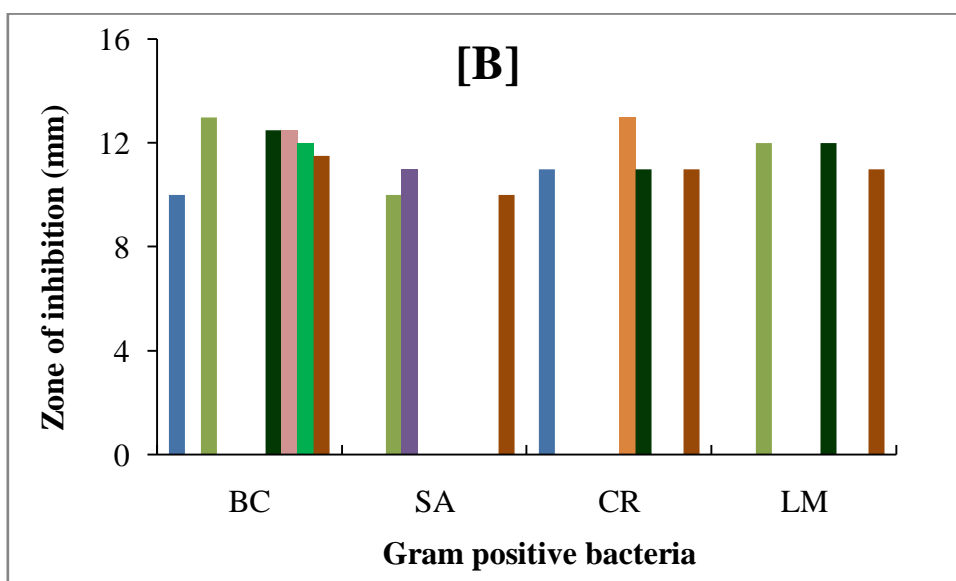
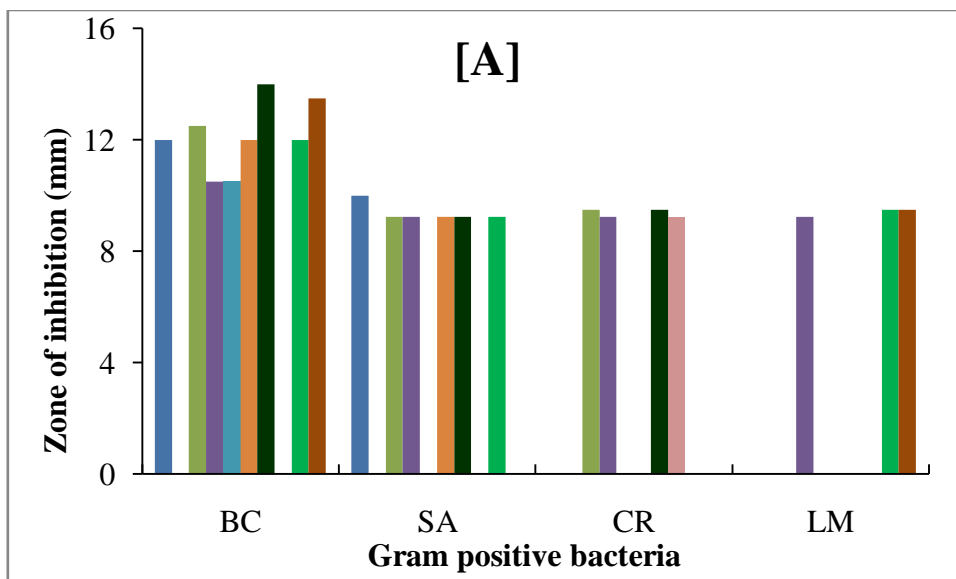
Thus, the zone of inhibition depends on solvent, bacterial strain and structure of compounds. All the studied compounds have the same central moiety but different substitution groups. Thus, in a particular solvent, substituent groups affect different strains. Table 4.1 shows the substitutions for the studied compounds KC-1 to KC-10.

Comparison of inhibition of compounds among four different strains suggests that in DMF (Figure 4.1 [A]), against BC, maximum inhibition of KC-7 is due to the presence of chloro group at 3rd (meta) position. The presence of methyl group at 4th (para) position (as in KC-10) is also effective. Both KC-2 and KC-8 containing methoxy groups at 4th and 3rd positions respectively, had no effect against BC. This suggests that methoxy groups at these positions are not effective. However, when two methoxy groups are present at both 3rd and 4th positions as in KC-5, it could inhibit BC. Thus, the position and number of groups also plays an important role. This is further confirmed by the fact that KC-7 having 3-chloro group exhibited maximum inhibition against BC but when chloro group is at 4th position as in KC-1, inhibition is decreased. Against SA, maximum inhibition is observed by KC-1 containing 4-

Figure 4.1: Zone of inhibition of pyrazolo quinazoline derivatives against Gram positive bacteria in [A] DMF and [B] DMSO.

KC-1: (■); KC-2: (■); KC-3: (■); KC-4: (■); KC-5: (■);

KC-6: (■); KC-7: (■); KC-8: (■); KC-9: (■); KC-10: (■).



chloro group. The methoxy groups are not effective at all for SA which is present in KC-2, KC-5 and KC-8. Against CR and LM, some other groups are also found to be effective moderately.

Figure 4.2 [A] shows antimicrobial activity of compounds against Gram negative bacterial strains in DMF. Out of four selected Gram negative bacteria, *Escherichia coli* (EC) and *Pseudomonas aeruginosa* (PA) are not affected by any of the synthesized compounds. Except KC-5, KC-6 and KC-9 all the studied compounds could inhibit *Salmonella typhimurium* (ST) and maximum inhibition is observed by KC-7. However, *Klebsiella pneumoniae* (KP) is inhibited by only KC-3, KC-4 and KC-10 and maximum inhibition is observed by KC-4.

Thus, against Gram negative bacteria also, side chain substitution affects inhibition. Against ST and KP, 3-chloro (as in KC-7) and 4-bromo (as in KC-4) respectively are found to be most effective. Thus, in DMF, EC and PA are the most resistant and ST is most susceptible bacteria.

Figure 4.2 [B] shows antimicrobial activity against Gram negative bacteria in DMSO. Not a single compound could inhibit EC. Against PA, only KC-2, KC-3, KC-8, KC-9 and KC-10 exhibited inhibition and maximum inhibition is observed by KC-9 containing 3-bromo group. Against ST and KP, only KC-4, KC-5, KC-8 and KC-9 showed inhibition and maximum inhibition is observed for KC-9.

Thus in DMSO, 3-bromo containing compound KC-9 is most effective which is followed by 3, 4-di methoxy (as in KC-5) and 3- methoxy (as in KC-8). Minimum effect is observed for KC-4 containing 4-bromo. This again proves important role of position of groups.

Comparison of inhibition of compounds between both the solvents shows that EC is the most resistant bacteria in both the solvents. PA could not inhibit by any compound in DMF whereas in DMSO, some compounds exhibited inhibition. Thus, solvent plays an important role.

The compounds KC-1 to KC-10 could not inhibit the zone of studied fungal strains in both the studied solvents.

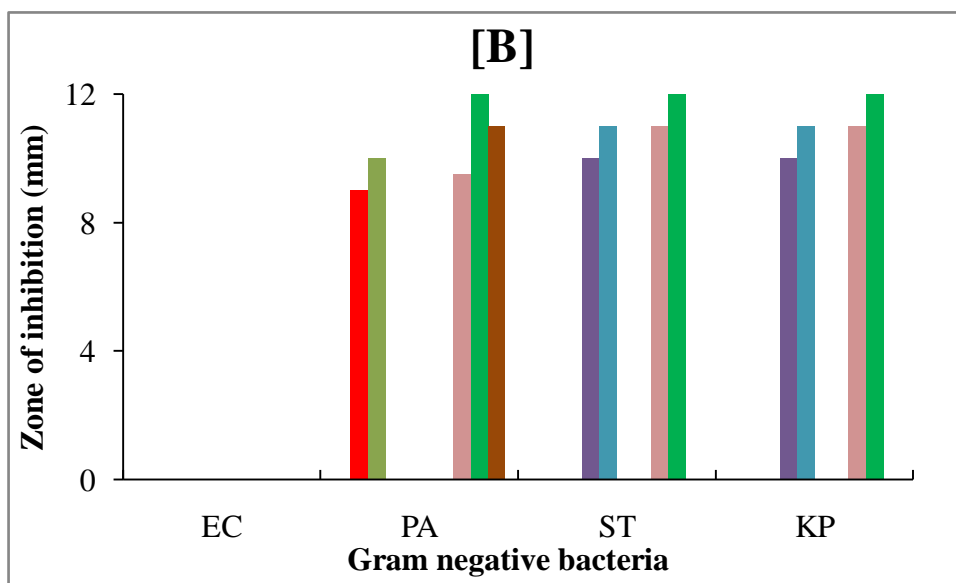
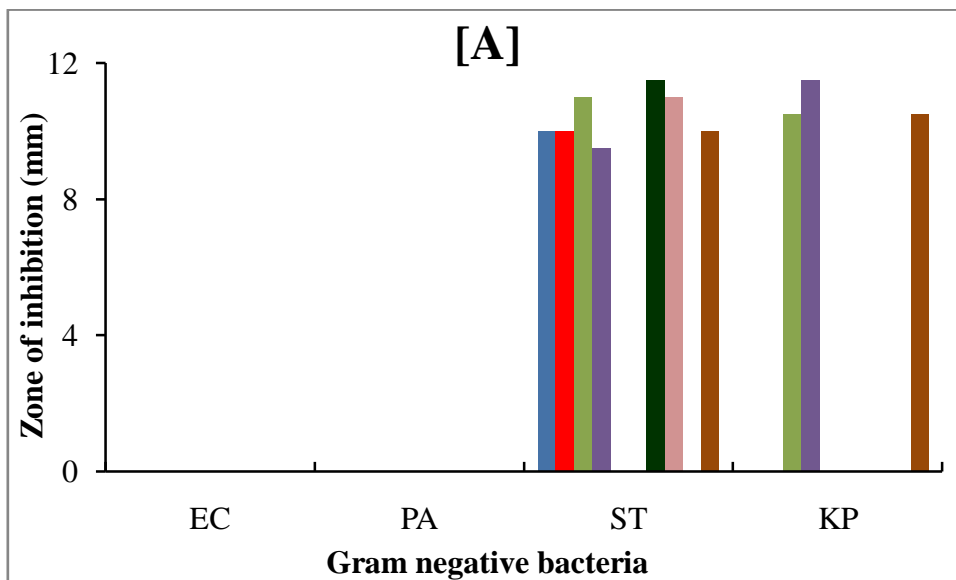
Table 4.1: Different substitutions for pyrazolo quinazoline derivatives.

Compound code	Substitution
KC-1	4-Cl
KC-2	-4-OCH ₃
KC-3	-4-F
KC-4	-4-Br
KC-5	-3,4-diOCH ₃
KC-6	-4-CN
KC-7	-3-Cl
KC-8	-3-OCH ₃
KC-9	-3-Br
KC-10	-4-CH ₃

Figure 4.2: Zone of inhibition of pyrazolo quinazoline derivatives against Gram negative bacteria in [A] DMF and [B] DMSO.

KC-1: (■); KC-2: (■); KC-3: (■); KC-4: (■); KC-5: (■);

KC-6: (■); KC-7: (■); KC-8: (■); KC-9: (■); KC-10: (■).



❖ *Schiff bases (ITA-1 to ITA-10):*

Figure 4.3 [A] shows zone of inhibition against Gram positive bacteria in DMF. It is observed that except ITA-4 and ITA-10, all the compounds could inhibit BC and maximum inhibition is observed by ITA-5. Against SA, only three compounds ITA-2, ITA-3 and ITA-5 showed inhibition. The maximum is observed by ITA-5 and minimum is by ITA-3. Only ITA-1, ITA-5 and ITA-7 could inhibit CR. However, LM is affected by only ITA-1. Other compounds had no effect on this bacterial strain. Thus, structure of compounds affects inhibition for different bacteria.

As all the compounds have the same central moiety their substitutions are different which affect inhibition. Table 4.2 shows substitution groups of all the synthesized compounds. Thus, it is observed that compounds containing nitro groups (ITA-4 having 3- nitro substitution and ITA-10 having 4- nitro substitution) are not effective at all against BC. Against SA, ITA-5 containing 4-bromo group is most effective which is followed by ITA-2 containing 2-hydroxy group. 4-flouro group (as in ITA-3) also inhibit SA to considerable extent. Other substitutions have no effect at all. The compound ITA-5 containing 4-bromo group exhibited maximum inhibition against CR whereas ITA-7 showed minimum inhibition which contains 4-methyl group. However, only ITA-1 containing 4-chloro group exhibited inhibition against LM. Thus in DMF, LM is the most resistant bacteria and BC is most susceptible bacteria.

Figure 4.3 [B] shows zone of inhibition against Gram positive bacteria in DMSO. Except ITA-3 and ITA-10 all the compounds could inhibit BC and maximum inhibition is observed by ITA-2 containing 2-hydroxy group. Thus, 4-fluoro and 4-nitro groups are not effective at all for BC, which are present in ITA-3 and ITA-10 respectively. Against SA, only few compounds exhibited inhibition and maximum is observed by ITA-9 containing 4-hydroxy group. ITA-3 containing 4-fluoro had minimum inhibition against SA. ITA-1, ITA-2 and ITA-9 could inhibit CR and again ITA-2 having 2-hydroxy group is most effective. This is followed by ITA-9 containing 4-hydroxy group. Thus, hydroxy group at either position is effective for CR. ITA-2, ITA-3, ITA-4 and ITA-9 showed moderate activity against LM and ITA-4 containing 3-nitro group is most effective. Thus, in DMSO, most of the compounds are effective against the selected Gram positive bacteria.

Figure 4.3: Zone of inhibition of Schiff bases against Gram positive bacteria in [A] DMF and [B] DMSO.

ITA-1: (■); ITA-2: (■); ITA-3: (■); ITA-4: (■); ITA-5: (■);
 ITA-6: (■); ITA-7: (■); ITA-8: (■); ITA-9: (■); ITA-10: (■).

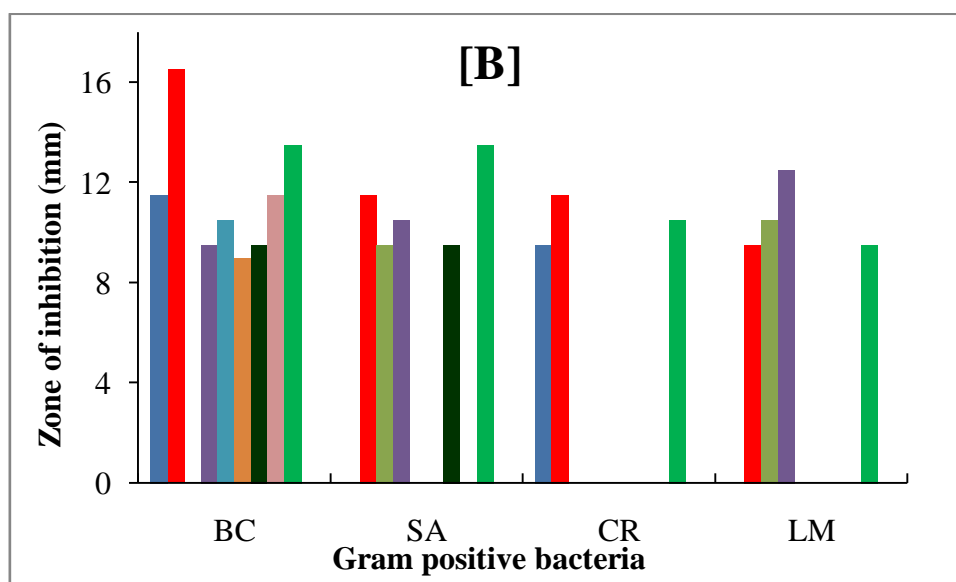
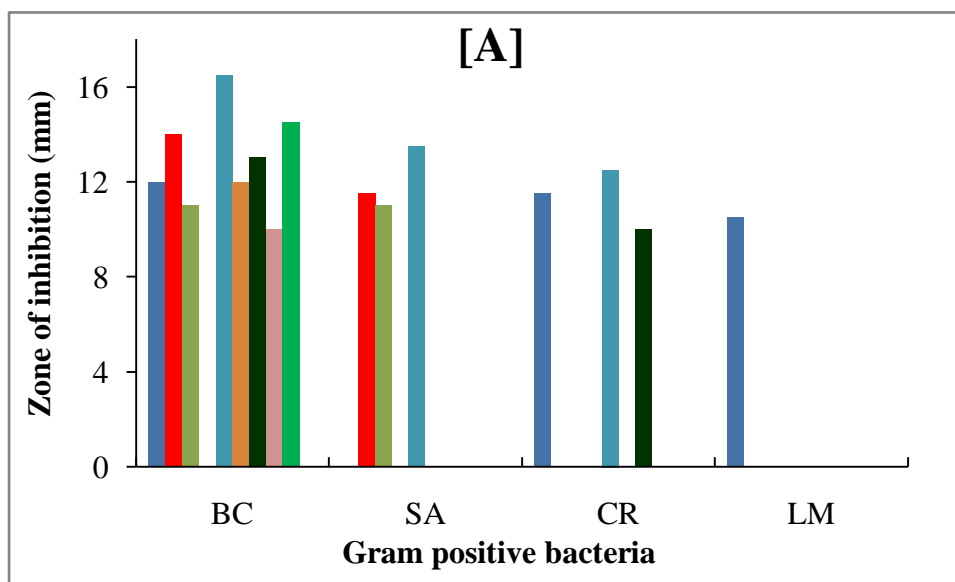


Table 4.2: Different substitutions for Schiff bases.

Compound code	Substitution
ITA-1	4-Cl
ITA -2	-2-OH
ITA -3	-4-F
ITA -4	-3-NO ₂
ITA -5	-4-Br
ITA -6	-4-OCH ₃
ITA -7	-4-CH ₃
ITA -8	-3, 4-diOCH ₃
ITA -9	-4-OH
ITA -10	-4-NO ₂

Comparison of inhibition in DMF and DMSO against selected Gram positive bacteria suggest that overall, there is not much effect of solvent on inhibition. Compound ITA-10 containing 4-nitro group is not effective at all in both the solvents.

Figure 4.4 [A] shows zone of inhibition against Gram negative bacteria in DMF. Against EC, only ITA-4 and ITA-5 containing 3-nitro and 4-bromo substitution respectively exhibited inhibition. The inhibition is higher for ITA-5 as compared to ITA-4. The rest of the compounds had no effect. Only, ITA-3 and ITA-9 having 4-flouro and 4- hydroxy substitution could inhibit PA. However, the inhibition is more in ITA-9 than ITA-3. The compounds ITA-1, ITA-6, ITA-7 and ITA-8 could not inhibit ST. About half of compounds (ITA-2, ITA-3, ITA-4, ITA-5, ITA-9 and ITA-10) could inhibit ST. ITA-3 and ITA-10 showed maximum inhibition in ST bacteria and ITA-4 showed minimum inhibition. Thus, 4-flouro and 4-nitro groups are more effective against ST as compared to other groups. Against KP, only compounds ITA-4, ITA-5 and ITA-9 showed inhibition and inhibition is maximum for ITA-5 and minimum for ITA-9. Thus, against 4-bromo group is most effective against KP. The compounds ITA-1, ITA-6, ITA-7, ITA-8 and ITA-10 could not inhibit the selected Gram negative bacteria. Thus, in DMF, EC and PA are resistant bacteria whereas ST is the most susceptible bacteria.

Figure 4.4 [B] shows inhibition of compounds against Gram negative bacteria in DMSO. Against EC, only half of the compounds exhibited inhibition and maximum is observed for ITA-5 having 4-bromo group. Only ITA-6, ITA-7 and ITA-9 could inhibit PA and maximum inhibition is observed for ITA-7 containing 4-methyl group. Against ST, again only half of the compounds ITA-1, ITA-2, ITA-6, ITA-7 and ITA-9 showed inhibition. Maximum inhibition is exhibited by ITA-1 and ITA-9 containing 4-chloro and 4-hydroxy groups respectively. Not a single compound could inhibit KP. Thus, KP is the most resistant bacteria in DMSO. Further, it is observed that in DMSO, compounds ITA-3, ITA-8 and ITA-10 were not effective against the selected Gram negative bacteria.

Over all, inhibition is higher in DMF as compared to DMSO. Further, against the studied Gram negative bacteria the compounds ITA-8 and ITA-10 are not effective at all in both the solvents.

Figure 4.5 shows zone of inhibition against some fungal strains in DMF and DMSO. In DMF (Figure 4.5 [A]), it is observed that only ITA-1 containing 4-chloro group showed inhibition against *Candida glabrata* (CG) fungal strain.

Figure 4.4: Zone of inhibition of Schiff bases against Gram negative bacteria in [A] DMF and [B] DMSO.

ITA-1: (■); ITA-2: (■); ITA-3: (■); ITA-4: (■); ITA-5: (■);
 ITA-6: (■); ITA-7: (■); ITA-8: (■); ITA-9: (■); ITA-10: (■).

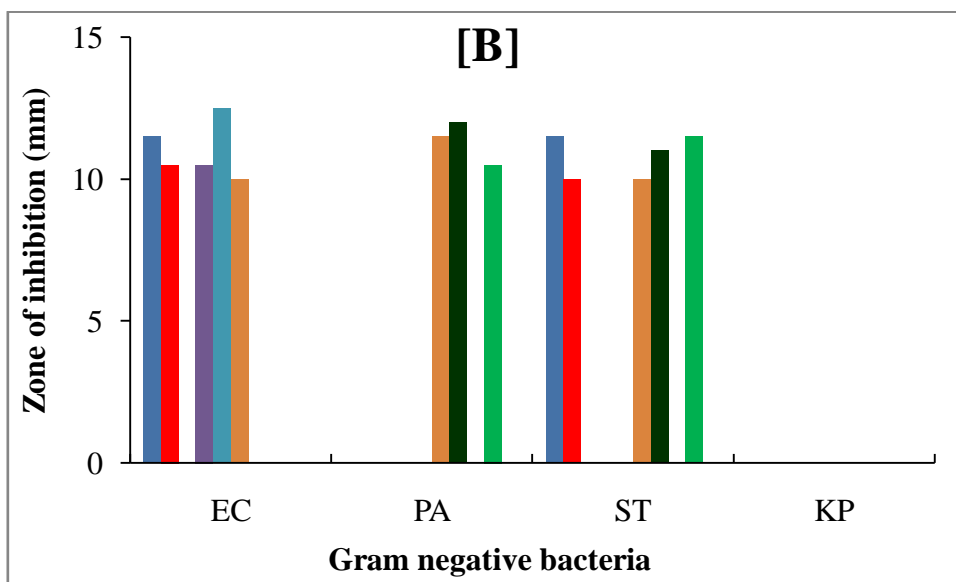
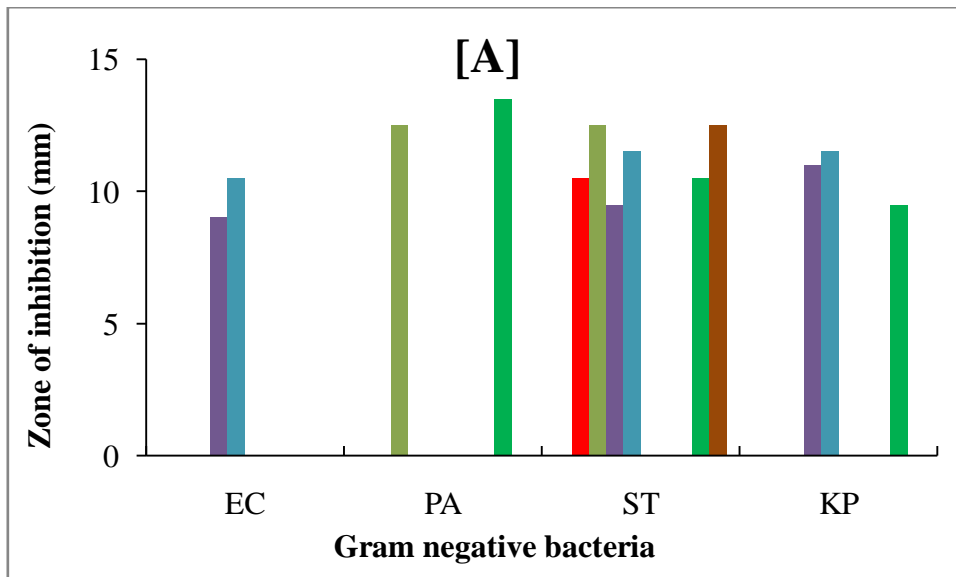
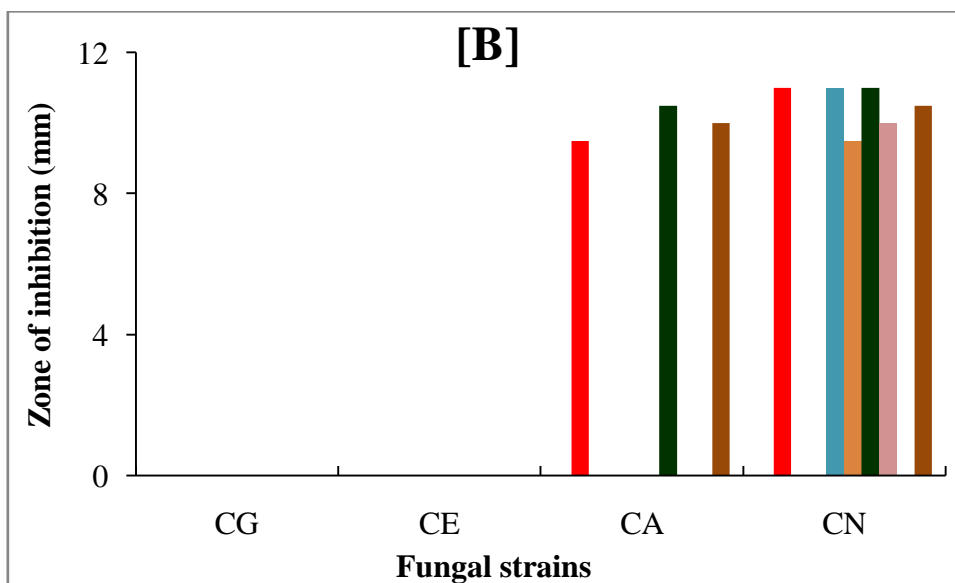
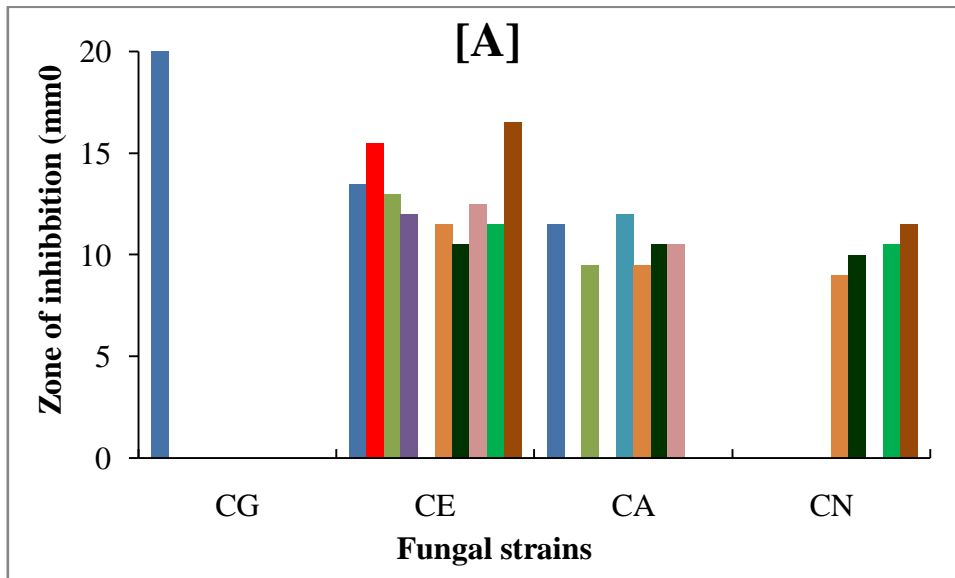


Figure 4.5: Zone of inhibition of ITA-1 to ITA-10 in [A] DMF and [B] DMSO.

ITA-1: (■); ITA -2: (■); ITA -3: (■); ITA -4: (■); ITA -5: (■);

ITA -6: (■); ITA -7: (■); ITA -8: (■); ITA -9: (■); ITA -10: (■).



Other compounds had no effect at all. However, against *Candida epicola* (CE), only ITA-5 having 4- bromo group is not effective. All other compounds show moderate activity against CE and maximum is exhibited by ITA-10 having 4- nitro group. For *Candida albicans* (CA), most of the compounds showed inhibition and maximum is observed for ITA-5. Only ITA-6, ITA-7, ITA-9 and ITA-10 could inhibit *Cryptococcus neoformans* (CN). Thus, 4-methoxy, 4-methyl, 4-hydroxy and 4-nitro groups are effective against CN and maximum effect is observed for ITA-10 containing 4- nitro group. It is observed from Table 4.2 that ITA-2 and ITA-4 contain 2-hydroxy and 3-nitro groups respectively. However, these compounds showed no inhibition against CN. This suggests that position of group is also important for inhibition. In DMF, CG is the most resistant fungal strain.

Figure 4.5 [B] shows inhibition of compounds against fungal strains in DMSO. Not a single compound could inhibit CG and CE fungal strain. Only three compounds i.e., ITA-2, ITA-7 and ITA-10 could inhibit CA and maximum inhibition is for ITA-7 containing 4-methyl group. For CN strain, ITA-2, ITA-5, ITA-6, ITA-7, ITA-8 and ITA-10 showed inhibition and maximum is for ITA-2, ITA-5 and ITA-7. Thus, 2-hydroxy, 4-bromo and 4-methyl groups are equally effective against this fungal strain. Thus, in DMSO, both CG and CE are resistant bacteria.

Comparison of inhibition in both the solvents suggests that for fungal strains also, solvent plays an important role in inhibition. Inhibition is higher in DMF than in DMSO. So DMF is good for solvent for the studied compounds in selected fungal strains.

❖ ***Cyano pyran derivatives (KHN-1 to KHN-10):***

Figure 4.6 [A] shows zone of inhibition against Gram positive bacteria in DMF for KHN-1 to KHN-10. In DMF, moderate inhibition was shown by some of the cyanopyran compounds. All the compounds have different substitution groups as listed in Table 4.3. Thus, substitution affects inhibition.

Against BC, only KHN-2, KHN-5 and KHN-7 showed inhibition and maximum inhibition is by KHN-2 having 4-hydroxy substitution. The 4-methoxy (as in KHN-5) and 4-chloro (as in KHN-7) groups also affect BC. KHN-6, KHN-7 and KHN-9 could inhibit SA and maximum inhibition is observed for KHN-9 having 2-methoxy group. The 4-chloro group present in KHN-7 had minimum effect for SA. Not a single compound could inhibit CR bacteria.

Figure 4.6: Zone of inhibition of KHN-1 to KHN-10 against Gram positive bacteria in [A] DMF and [B] DMSO.

KHN-1: (■); KHN -2: (■); KHN -3: (■); KHN -4: (■); KHN -5: (■);
 KHN -6: (■); KHN -7: (■); KHN -8: (■); KHN -9: (■); KHN -10: (■).

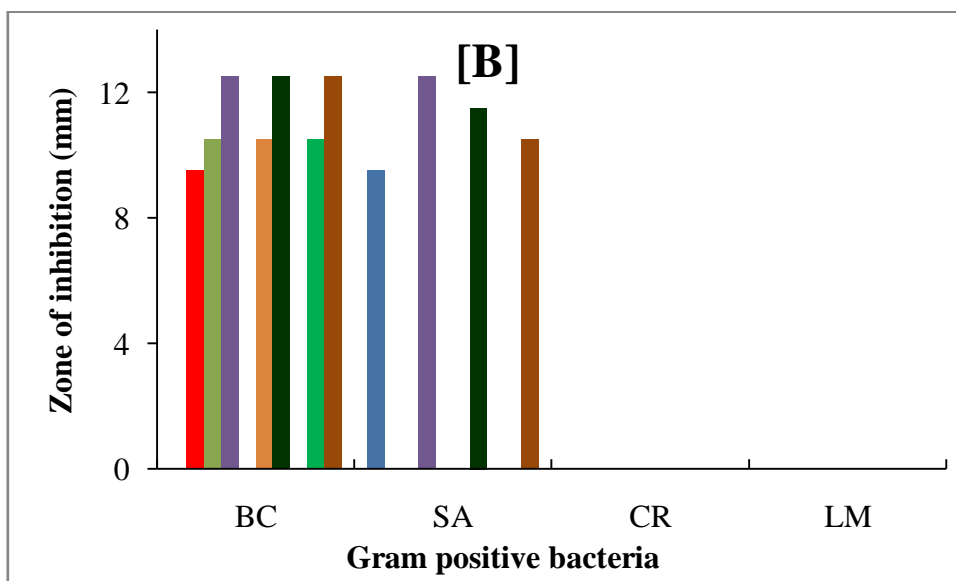
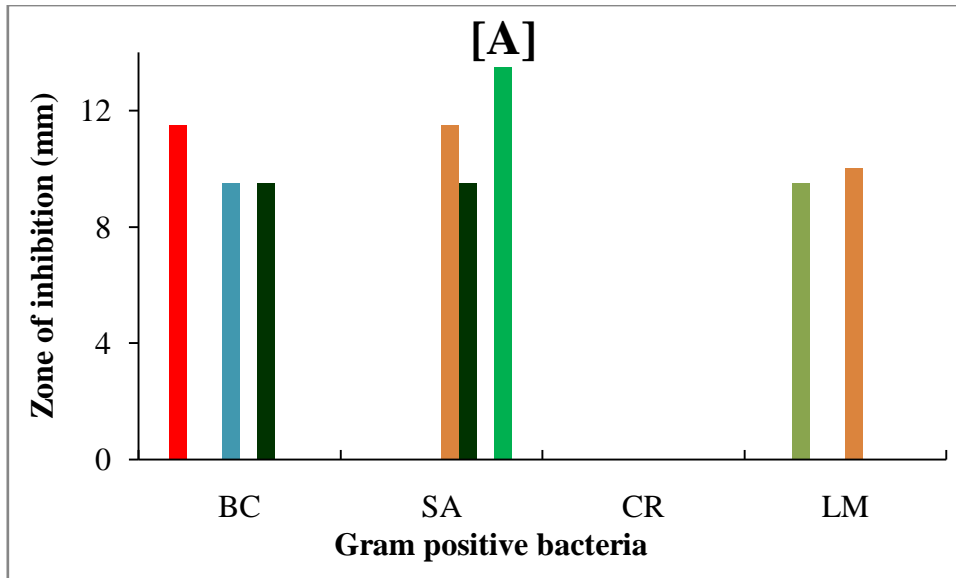


Table 4.3: Different substitutions for cyanopyran derivatives.

Compound code	Substitution
KHN-1	4-Br
KHN -2	-4-OH
KHN -3	-3, 4-diOCH ₃
KHN -4	-4-NO ₂
KHN -5	-4-OCH ₃
KHN -6	-3-NO ₂
KHN -7	4-Cl
KHN -8	-4-CH ₃
KHN -9	-2-OCH ₃
KHN -10	4-F

Thus, CR bacterium is most resistant bacteria. KHN-3 and KHN-6 could inhibit LM bacteria. KHN-3 having 3, 4-dimethoxy group whereas KHN-6 having 3-nitro group. Higher inhibition is shown by KHN-6 and lower inhibition is shown by KHN-3 in LM. KHN-1, KHN-4, KHN-8 and KHN-10 were not effective in DMF. Thus, it is observed that compounds containing 4-bromo group, 4-nitro group, 4-methyl group and 4-fluoro group are not effective at all against all the studied Gram positive bacteria in DMF.

Figure 4.6 [B] for the zone of inhibition against Gram positive bacteria in DMSO. For BC, except KHN-1, KHN-5 and KHN-8, the rest compounds show ed inhibition. For BC, the maximum inhibition is observed for compounds KHN-4, KHN-7 and KHN-10. Only four compounds, KHN-1, KHN-4, KHN-7 and KHN-10 could inhibit SA. KHN-4 shows maximum inhibition and KHN-1 shows minimum inhibition for SA bacteria. For SA bacteria, halogen groups are effective. None of the compounds could inhibit CR and LM. In DMSO, KHN-5 (containing 4-methoxy group) and KHN-8 (containing 4-methyl group) is not effective against all the studied Gram negative bacteria

Figure 4.7 [A] shows zone of inhibition against Gram negative bacteria in DMF. KHN-2 having 4-hydroxy substitution, KHN-5 having 4-methoxy substitution and KHN-8 having 4-methyl substitution could inhibit EC. However, maximum inhibition is observed for the compound KHN-2 whereas minimum inhibition is observed for the compound KHN-5. Only KHN-1 and KHN-7 containing 4-bromo and 4-hydroxy groups respectively, could inhibit PA. Between the two compounds, KHN-1 shows higher inhibition and KHN-7 shows lower inhibition. Only KHN-3 contains 3, 4-dimethoxy group could inhibit ST. The compound KHN-7 having 4-chloro group could inhibit KP.

Figure 4.7 [B] shows zone of inhibition of Gram negative bacteria in DMSO. KHN-2, KHN-3 and KHN-7 containig 4-hydroxy group, 3, 4-dimethoxy and 4-chloro groups could inhibit EC. In EC, maximum inhibition is shown in KHN-2 whereas minimum inhibition is shown in KHN-3. KHN-6 having 3-nitro group could inhibit PA. The rest of the compounds could not inhibit PA. KHN-10 containing 4-fluoro

Figure 4.7: Zone of inhibition of KHN-1 to KHN-10 against Gram negative bacteria in [A] DMF and [B] DMSO.

KHN-1: (■); KHN -2: (■); KHN -3: (■); KHN -4: (■); KHN -5: (■);

KHN -6: (■); KHN -7: (■); KHN -8: (■); KHN -9: (■); KHN -10: (■).

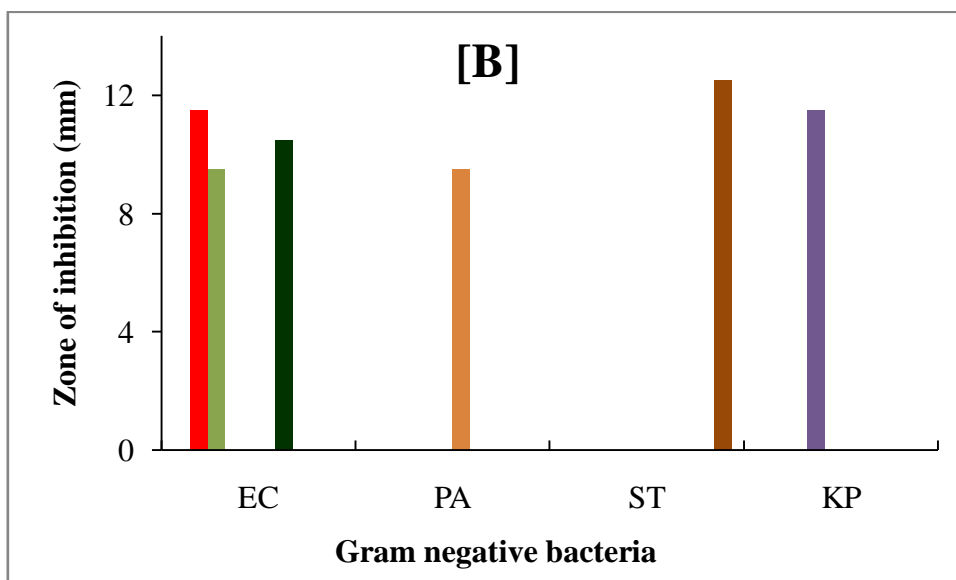
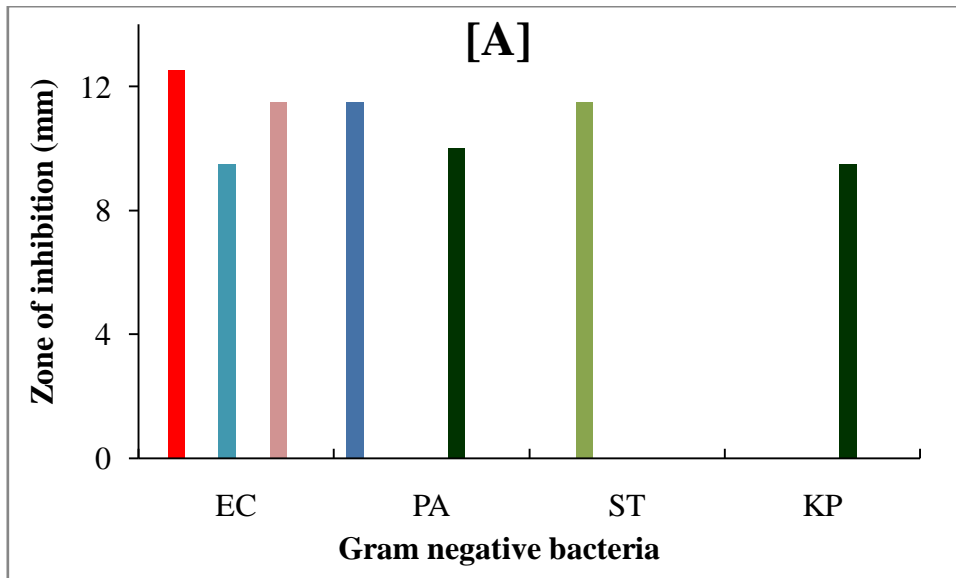
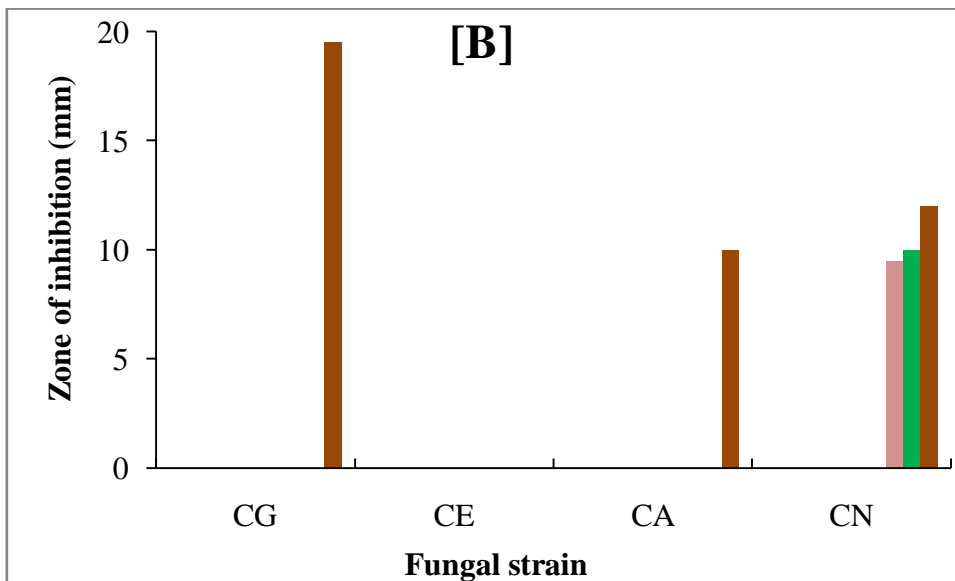
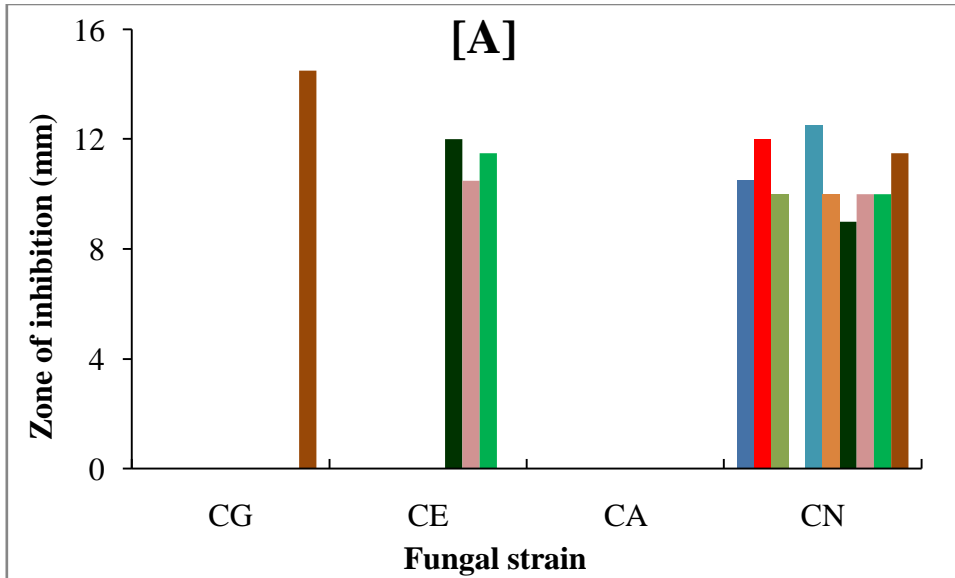


Figure 4.8: Zone of inhibition of KHN-1 to KHN-10 against fungi in [A] DMF and [B] DMSO.

KHN-1: (■); KHN -2: (■); KHN -3: (■); KHN -4: (■); KHN -5: (■);

KHN -6: (■); KHN -7: (■); KHN -8: (■); KHN -9: (■); KHN -10: (■).



group could inhibit ST. Only KHN-4 having 4-nitro group could inhibit KP. Thus, it is shown that KHN series could not inhibit more Gram negative bacteria in both the studied solvents.

Figure 4.8 [A] shows activity of KHN-1 to KHN-10 against fungal strain in DMF. Only KHN-10 (4-flouro group) could inhibit CG. KHN-7, KHN-8 and KHN-9 could inhibit CE which have 4-chloro group, 4-methyl and 2-methoxy substitutions respectively. KHN-7 shows maximum inhibition whereas KHN-8 shows minimum inhibition. Not a single compound could inhibit CA. Most of the compounds (except KHN-4) showed moderate inhibition against CN. Maximum inhibition is shown for KHN-5 (4-methoxy group) and minimum inhibition is shown by KHN-8 (4-methyl group).

Figure 4.8 [B] show zone of inhibition against fungal strains in DMSO. Only KHN-10 having 4-flouro group could inhibit CG and CA. KHN-8, KHN-9 and KHN-10 could inhibit CN. Maximum inhibition is shown by KHN-10 and minimum inhibition is shown by KHN-8. None of the compound could inhibit CE.

Over all, more compounds exhibited inhibition in DMF.

❖ *Pyrimidine derivatives (AMG-1 to AMG-10):*

Figure 4.9 shows the zone of inhibition of synthesized compound against Gram positive bacteria in DMF and DMSO. In DMF (Figure 4.6 [A]), against BC AMG-5 exhibited maximum inhibition and minimum is shown by AMG-4. The compounds AMG-1, AMG-6 and AMG-8 showed moderate inhibition against BC. Other compounds had no effect at all. In DMSO, against BC, AMG-1 had maximum inhibition whereas minimum inhibition is due to AMG-6. Some of the compounds had no effect all against BC. The results suggest that inhibition depends not only on structure of compounds but also on the solvent. Against BC, in DMF, maximum compounds had inhibition as compared to DMSO. So, for this strain, DMF is more effective. The comparison of inhibition among different compounds shows that all the compounds have the same central moiety but different substitution groups as shown in Table 4.4.

In DMF, AMG-5 containing 4-methoxy group showed maximum inhibition against BC. AMG-8 also contains methoxy group but at 3rd position but its effect is less as compared to AMG-5. This suggests that position of group also affect inhibition. In DMSO, against BC AMG-1 containing 4-chloro group had maximum

Figure 4.9: Zone of inhibition of compounds AMG-1 to AMG-10 against Gram positive bacteria in [A] DMF and [B] DMSO.

AMG-1: (■); AMG -2: (■); AMG -3: (■); AMG -4: (■); AMG -5: (■);
 AMG -6: (■); AMG -7: (■); AMG -8: (■); AMG -9: (■); AMG -10: (■).

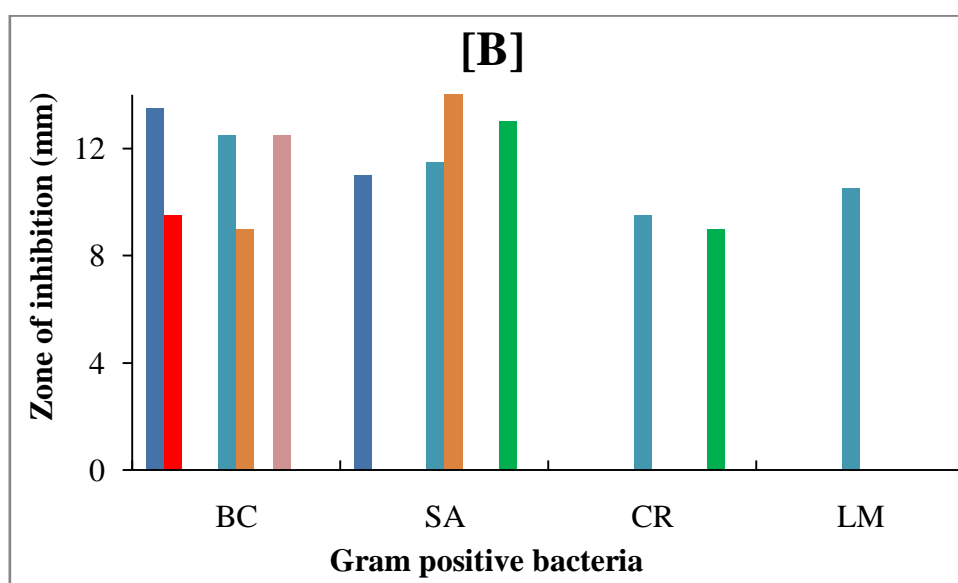
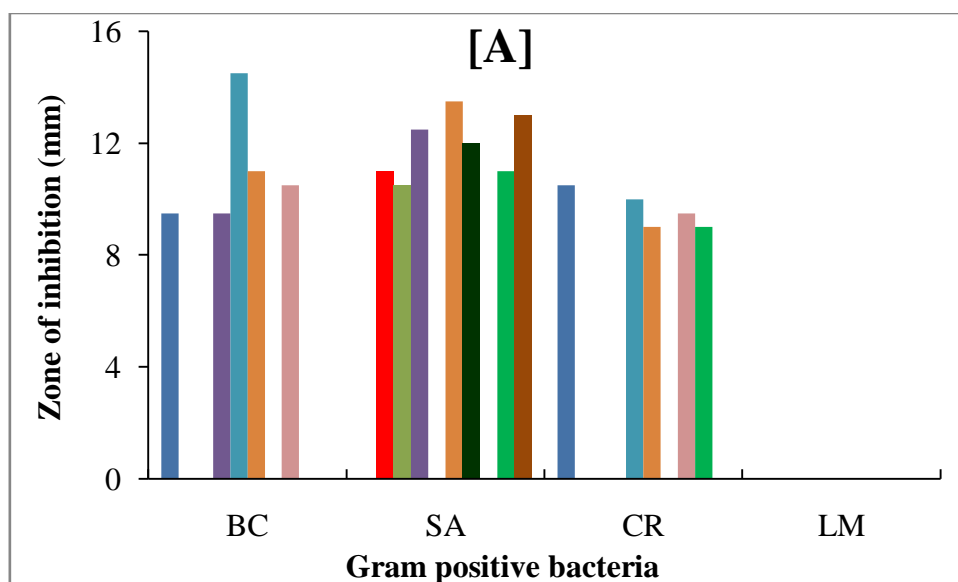


Table 4.4: Different substitutions for pyrimidine derivatives.

Compound code	Substitution
AMG-1	4-Cl
AMG -2	-3, 4-diOCH ₃
AMG -3	3-Cl
AMG -4	4-Br
AMG -5	-4-OCH ₃
AMG -6	4-F
AMG -7	-4-CH ₃
AMG -8	-3-OCH ₃
AMG -9	Thiophene
AMG -10	-2, 5-diOCH ₃

effect but when chloro group is at 3rd position as in AMG-3, it had no effect at all. Against SA, AMG-6 exhibited maximum inhibition in DMF whereas AMG-3 had minimum inhibition. Other compounds showed moderate inhibition except AMG-5 and AMG-8. Thus, in DMF against this strain 4-fluoro group is very effective whereas methoxy group at 3rd and 4th position had no effect at all. However, in DMSO against SA, only AMG-1, AMG-5, AMG-6 and AMG-9 showed inhibition and maximum is exhibited by AMG-6 containing 4-fluoro group. The comparison of inhibition against this strain in the two solvents again suggests DMF to be good solvent. AMG-1, AMG-5, AMG-6, AMG-8, and AMG-9 could inhibit CR in DMF and effect is maximum for AMG-1 containing 4-chloro group. In DMSO, only AMG-5 containing 4-methoxy and AMG-9 containing thiophene inhibit CR. For LM, not a single compound was effective in DMF whereas in DMSO, only AMG-5 exhibited inhibition.

Over all, AMG-6 (containing 4-fluoro group) could inhibit 75% of Gram positive bacteria in DMF solvent and AMG-5 could inhibit 100% the zone of inhibition in DMSO. Thus, AMG-5 having 4-methoxy substitution is more effective for studied Gram positive bacteria in both the solvents and DMF is good solvent for the studied Gram positive bacteria.

Figure 4.10 shows zone of inhibition against Gram negative bacteria in DMF and DMSO. Only AMG-2 and AMG-3 containing 3, 4-dimethoxy and 3-chloro groups respectively inhibit EC in DMF whereas AMG-6 and AMG-8 containing 4-fluoro and 3-methoxy groups respectively could inhibit EC in DMSO. Thus, position of group and solvent affect inhibition.

Against PA, only one compound AMG-8 containing 3-methoxy group showed inhibition in DMF whereas in DMSO, AMG-2 and AMG-3 exhibited inhibition. Thus, in DMSO, 3, 4-dimethoxy and 3-chloro groups are effective.

In DMF, against ST only AMG-1 and AMG-10 showed inhibition and maximum inhibition is by AMG-1 containing 4-chloro group. AMG-2, AMG-4, AMG-6 and AMG-8 could inhibit ST in DMSO and 3,4-dimethoxy group present in AMG-2 is most effective.

In DMF, AMG-4, AMG-8 and AMG-9 showed inhibition against KP and maximum inhibition is by AMG-4 containing 4-bromo group. None of the compound could inhibit KP in DMSO.

Figure 4.10: Zone of inhibition of compounds AMG-1 to AMG-10 against Gram negative bacteria in [A] DMF and [B] DMSO.

AMG-1: (■); AMG-2: (■); AMG-3: (■); AMG-4: (■); AMG-5: (■);
 AMG-6: (■); AMG-7: (■); AMG-8: (■); AMG-9: (■); AMG-10: (■).

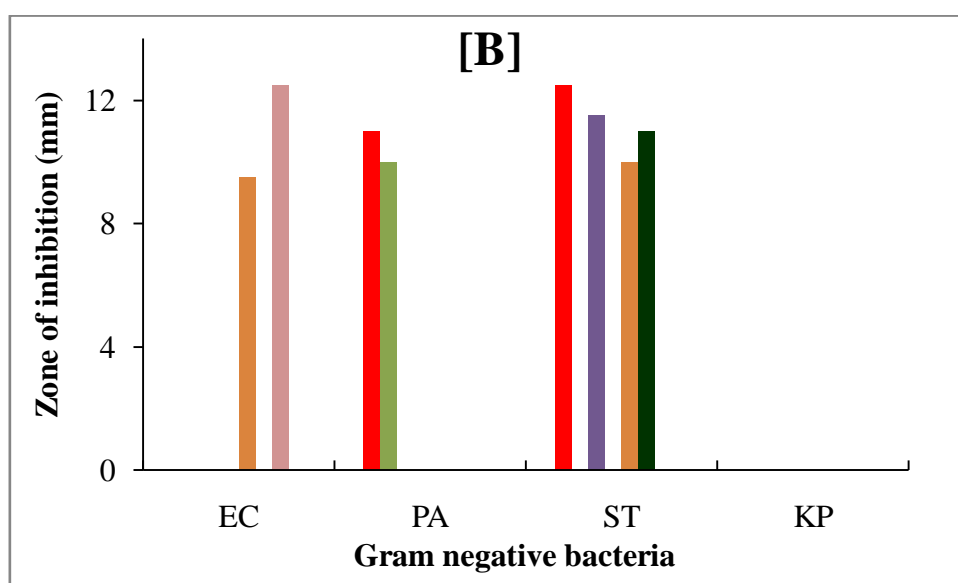
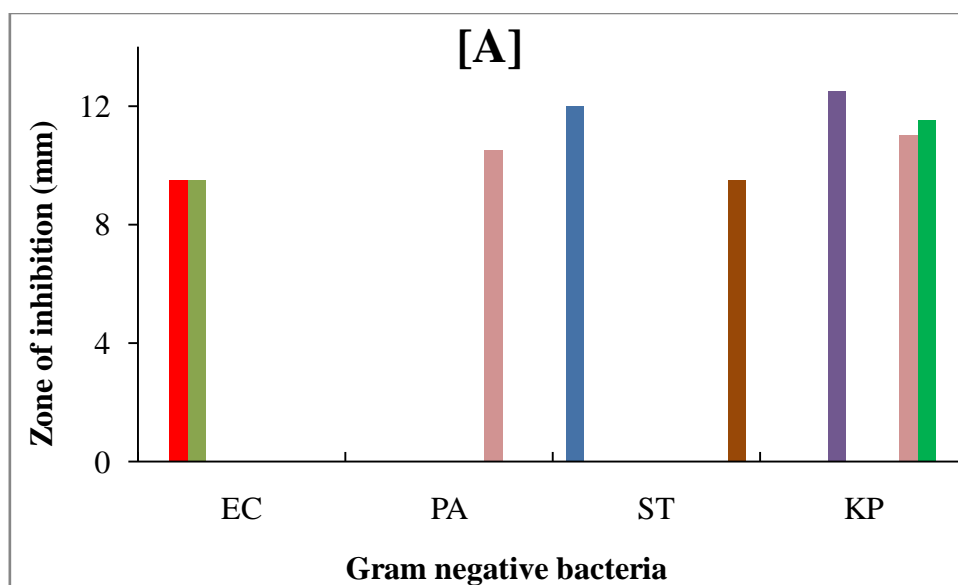
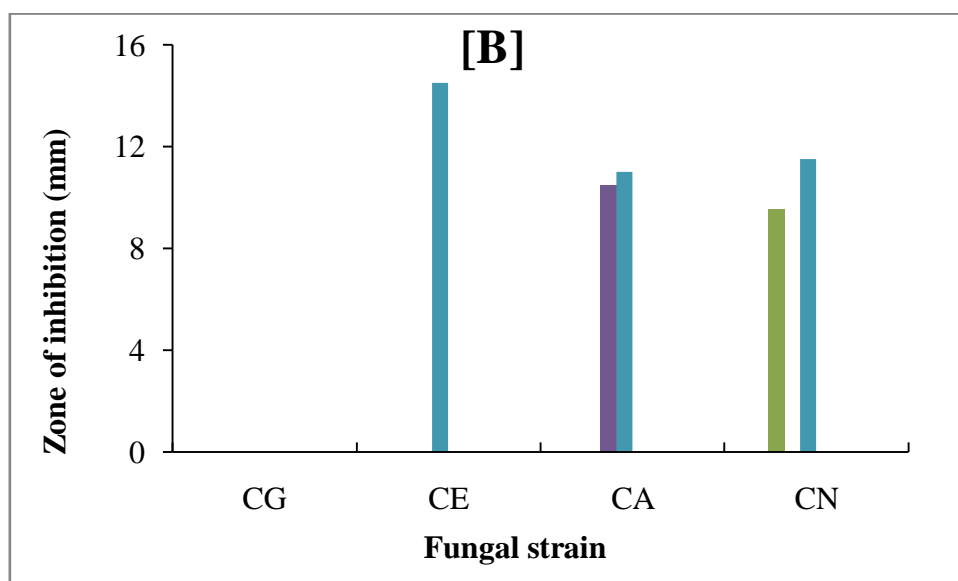
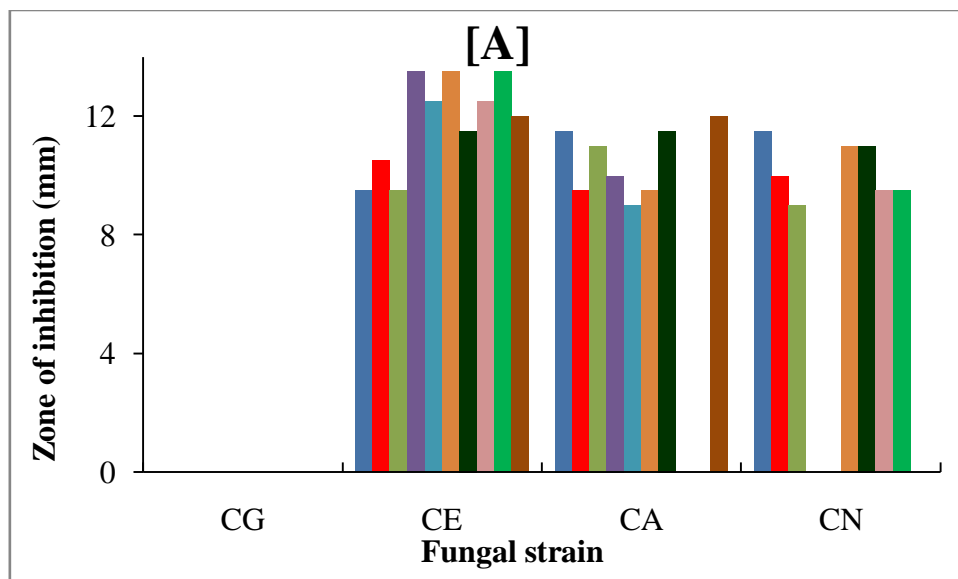


Figure 4.11: Antifungal activity of compounds AMG-1 to AMG-10 in [A] DMF and [B] DMSO.

AMG-1: (■); AMG -2: (■); AMG -3: (■); AMG -4: (■); AMG -5: (■);
 AMG -6: (■); AMG -7: (■); AMG -8: (■); AMG -9: (■); AMG -10: (■);



Thus, among studied Gram negative bacteria, for the studied compounds, DMSO is better solvent and KP is the most resistant bacteria. Further, the studied compounds are found to be not as effective against Gram negative bacteria as compared to Gram positive bacteria.

The zones of inhibition against four fungal strains are shown in Figure 4.11 for all the compounds in DMF and DMSO. Not a single compound could inhibit CG in both DMF and DMSO. Thus, CG is most resistant fungal strain among the selected fungal strains for the studied compounds.

All the studied compounds show moderate activity against CE in DMF whereas only AMG-5 containing 4-methoxy group inhibited CE in DMSO. So, methoxy group at 4th position is more effective for CE in DMSO whereas all the groups are effective in DMF.

Except AMG-8 and AMG-9, all the studied compounds showed inhibition against CA in DMF. Only AMG-4 and AMG-5 could inhibit CA in DMF. Against CN, all the compounds except AMG-4, AMG-5 and AMG-10, exhibited inhibition in DMF. However, in DMSO, only AMG-3 and AMG-5 could inhibit.

AMG-5 containing 4-methoxy group could inhibit 75% zone of inhibition in both the solvents. AMG-6 containing 4-flouro group could inhibit 75% of the studied fungal strains in DMF whereas in DMSO, this compound had no effect at all.

Again, for the studied fungal strains, DMF is better solvent.

Thus, it is concluded that the antimicrobial activity depends on three S:

Strain
Solvent
Structure.

REFERENCES

1. M. M. Khafagy, A. H. F. A. El-Wahas, F.A. Eid, A.M. El-Agrody, Synthesis of halogen derivatives of benzo[a]anthracene with promising antimicrobial activities, *Farmaco.*, 57 (2002) 715-722.
2. J. Skommer, D. Wlodkowic, M. Matto, M. Eray, J. Pelkonen, HA14-1, a small molecule Bcl-2 antagonist, includes apoptosis and modulates action of selected anticancer drugs in follicular lymphoma B cells, *Leukemia Res.*, 30 (2006) 322-331.
3. A. A. Patchett, R. P. Nargund, Privileged structures-an update, *Annu. Rep. Med. Chem.*, 35 (2000) 289-298.
4. A. Kumar, S. Sinha M. S. Chauhan, Synthesis of novel antimyco-bacterial combinatorial libraries of structurally diverse substituted pyrimidines by three-component solid phase reactions, *Bioorg. Med. Chem. Lett.*, 12 (2002) 667-670.
5. P. G. Baraldi, M. G. Pavani, M. Nunez, P. Brigidi, B. Vitali, R. Gambari and R. Romagnoli, Antimicrobial and antitumor activity of *N*-heteroimine-1,2,3-dithiazoles and their transformation in triazolo-, imidazo- and pyrazolopyrimidines, *Bioorg. Med. Chem.*, 10 (2002) 449-456.
6. M. N. Nasr M. M. Gineinah, Pyrido 2, 3-d pyrimidines and pyrimido 5',4':5,6 pyrido 2,3-d pyrimidines as new antiviral agents: Synthesis and biological activity, *Arch. Pharm.*, 335 (2002) 289-295.
7. N. Kumar, G. Singh A. K. Yadav, Synthesis of some new pyrido 2,3-d pyrimidines and their ribofuranosides as possible antimicrobial agents, *Heteroat. Chem.*, 12 (2001) 52-56.
8. O. Bruno, C. Brullo, S. Schenone, A. Ranise, F. Bondavalli, E. Barocelli, M. Tognolini, F. Magnanini, V. Bollabeni, Progress in 5H-1 benzopyrano 4,3-d pyrimidin-5-amine series: 2-methoxy derivatives effective as antiplatelet agents with analgesic activity, *Farmaco.*, 57 (2002) 753-758.
9. C. Mustazza, M. R. D. Guidice, A. Borioni F. Gatta, Synthesis of pyrazolo 1,5-a-1,2,4-triazolo 1,5-a-and imidazo 1,2-a pyrimidines related to Zaleplon, a new drug for the treatment of insomnia, *J. Heterocycl. Chem.*, 38 (2001) 1119-1130.
10. C. A. Lipinski, F. Lombardo, B. W. Dominy, P. J. Feeney,. Experimental and computational approaches to estimate solubility and permeability in drug discovery and development settings, *Adv Drug Deliv Rev*, 46 (2001) 3-26.

11. K. R. Valasani, J. R. Vangavaragu, V. W. Day, S. S. Yan, Structure based design, synthesis, pharmacophore modeling, virtual screening, and molecular docking studies for identification of novel cyclophilin d inhibitors, *J Chem. Inf. Model.*, 24 (2014) 902-912.
12. L. Zhang, H. Zhu, T. I. Oprea, A. Golbraikh, A. Tropsha, QSAR Modeling of the Blood–Brain Barrier Permeability for Diverse Organic Compounds, *Pharm. Res.*, 25 (2008) 1902-1914.
13. V. A. Palyulin, E. V. Radchenko, N. S. Zefirov, Molecular Field Topology Analysis Method in QSAR Studies of Organic Compounds, *J. Chem. Inf. Comput. Sci.*, 40 (2000) 659-667.
14. B. I. Escher, R. P. Schwarzenbach, Mechanistic studies on baseline toxicity and uncoupling of organic compounds as a basis for modeling effective membrane concentrations in aquatic organisms, *Aquat. Sci.* 64 (2002) 20–35.
15. K. Hugo; QSAR and 3D QSAR in drug design Part-2 applications and problems, *Drug Design*, 2(12), 538 (1997).
16. D. Cheg, Relationship of quantitative structure and pharmacokinetics in fluoroquinolone antibacterials, *World J Gastroenterol*, 13(17) (2007) 2496
17. T. Langer and S. Bryant, 3D Quantitative structure–property relationships, *The Practice of Med. Chem.*, 3 (2008) 587-604.
18. J. A. Riddick, W. B. Bunger, T. Sakano, *Organic solvents-physical properties and methods of purification, techniques of chemistry*, New York, (1986).
19. J. Parekh, P. Inamdar, R. Nair, S. Baluja, S. Chanda, Synthesis and antibacterial activity of some Schiff bases derived from 4-amino benzoic acid, *J. Serb. Chem. Soc.*, 70 (2005) 1155- 1161.