Synthesis of Pyrimidine derivatives of Medicinal Importance

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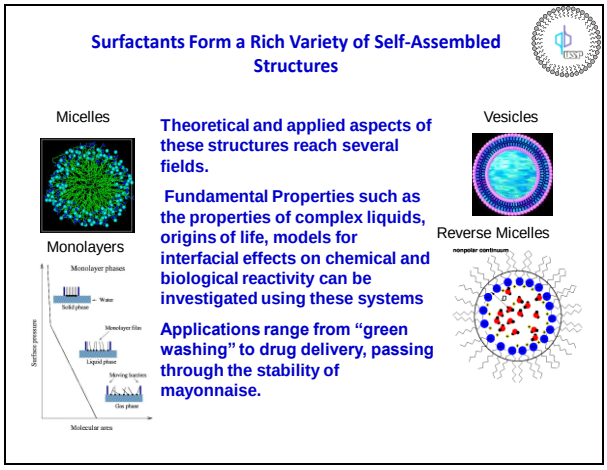
INTRODUCTION

Many pyrimidine derivatives are pharmacologically important as calcium channel blockers, antihypertensive agents[1]. Liposomes (Scheme 1) are increasingly being considered as drug carriers[2]. Five member heterocyclic compounds, 5HC, in principle, can be incorporated into liposomes both in the membranes and in the internal aqueous compartment[2,3]. 5HC´s show various types of biological activities, i.e., 2,5-di substituted 1,3,4-thiadiazoles are associated with diverse biological activities, probably by the virtue of N=C-S- grouping, similarly, 2,5-disubstituted 1,3,4-oxadiazoles also display wide spectrum of interesting pharmacological activities[1]. In this communication we present the synthesis of several new liposomes incorporable, potentially useful 5HC´s (Scheme **2**).

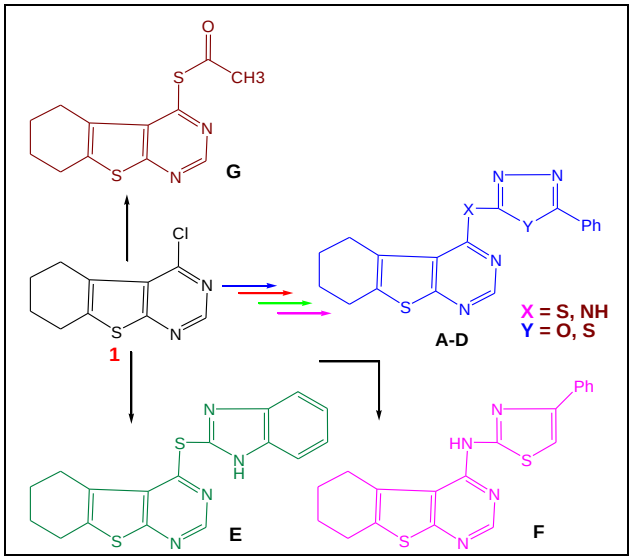
RESULTS AND DISCUSSION

The starting intermediate Benzothieno[2,3-d] pyrimidine,4-chloro-5,6,7,8-tetrahydro-compound (**1**) in Scheme-**2** was prepared from a mixture of cyclohexanone, ethyl cyanoacetate, diethyl amine and sulfur in the presence ethanol at 40^{0}C, then cyclisation with ammonium acetate in formamide followed by chlorination with $POCl_3$ in DMF at 110^{o}c with 90% yield and m.p.109-111^{0}c. The other intermediates, 5-phenyl-1,3,4-oxa / thiadiazole-2-thiol, 5-phenyl-1,3,4-oxa / thiadiazole-2-amine and Thio bezimidazole were prepared as followed literature procedures. Compound **1** was reacted with such intermediates in the presence of K_2CO_3 in DMF at refluxing conditions gave new pyrimidine derivatives (**A-E**). Similarly Compound **1** was reacted with phenyl amino thiazole and thioacetic acid in the presence of NaH in DMF at r. t. gave new **F** and **G** compounds. The compounds **A-D** had yield 85% and m. p. 250-252^{0}C (X=S, Y=O), with yield 78% and m. p. 175-177 (X=S, Y=S), yield 80%, m. p. 240-243 ^{0}C, (X=NH, Y=O) yield 88% and mp.145-147 ^{0}C (X=NH, Y=S) respectively. Likewise, the compound **E** had 65% yield and m. p. 152-154^{0}C and, **F** had yield 72% m. p. 178-181^{0}C and compound **G** yield 78% and m.p.150-152 ^{0}C, respectively. In the H^{1}NMR ($CDCl_3$, 500Mz) of compounds **C** and **D**, N-*H* peak were observed at *δ* 12.2-12.5 ppm and the compounds ***E*** and ***F,*** N-*H at δ* 11.7 -12.3 ppm. The methyl proton was observed at *δ 2.3 ppm* in compound **G**, beside signal exhibit in aromatic regions. The structures of the compounds were further established by IR, ^{13}C NMR and mass spectroscopy.

Scheme.1



Scheme.2



CONCLUSION

Several new compounds was prepared from (1) Benzothieno (2,3-d) pyrimidine, 4-chloro-5,6,7,8-tetrahydro compound followed by biological activity carried out like that antimicrobial, vesicles and micelles activity.

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