1.7 Aim of investigation

In reviewing various structural features of different drugs or compounds under investigation as angiogenesis inhibitors. Utilization of fractional base analysis in drug design, we invision the synthesis of aminoacetylenic derivatives of 2-methyl indoline as shown in (figure 18) for the following reasons:

1. 2-methyl indoline is an isoster or fractional base analogue to phthalimide in thalidomide and to indolone in lenalidomide.
2. Replacement of glutarimide in thalidomide and lenalidimide by unique aminoacetylenic group to avoid teratogenicity and side effects associated with thalidomide and lenalidomide.
3. Aminoacetylenic moiety provide the appropriate functional groups that provide the required overlap with EGF receptor that generate antagonistic activity as follow:

a) Amino group for ionic or hydrogen bonding with corresponding groups on different amino acid components of EGF receotor, as confirmed in molecular docking.

b) Acetylenic group for electrostatic interaction with π-overlap located on the EGF receptor.

c) 2-butyne to provide specific and appropriate distance between the indoline and the cyclic amino group.

d) Non bonding charge transfare between acetylenic bond and 2-methylindoline in our compounds with various hydrogen donating groups located in the EGF receptor.

The above points clearly indicate our reasonable prediction to synthesize EGFR antagonist.