# Abstract

This thesis comprises four chapters. The first one is an introduction which consists of a brief survey on the different methods to synthesize quinoline containing compounds and their anticancer activity, in addition to antimicrobial activity.

The second chapter deals with the aim of the work and Schemes that have been carried out to obtain the new required quinoline derivatives.

The third chapter clarifies the theoretical discussion of the experimental work for the preparation of the new enamine compounds **IIIa-e.** Amide compounds **IVa-d** formed from reaction of the acid chloride derivatives which resulted from **IIIc&d** *in situ* with different aromatic amines. Cyclization of compounds **IIIa-e** to quinoline derivatives **VIa-d** in boilied diphenylether was done and then subjected to chlorination to give the key 4-chloro quinoline intermediates **VIIa-d**. Reaction of compounds **VIIa&d** with hydrazine hydrate or phenyl hydrazine resulted in formation of pyrazolo quinoline derivatives **VIII** and **IXa&b**. In addition to the synthesis of the target 4-aminoquinoline compounds **Xa-l** by reaction of **VIIa-d** with different aromatic amines.

Hydrolysis of diethyl-8-bromo-4-(p-substitutedamino)quinoline-3,6-dicarboxylate **Xg-Xi** by sodium hydroxide resulted in formation of 8-bromo-4-(p-substitutedamino)quinoline-3,6-dicarboxylic acid compounds **XIa-c**.

Claisen –Schmidt condensation of diethyl 4-((4-acetylphenyl)amino)-8-bromoquinoline-3,6-dicarboxylate (**Xk)** with different aromatic aldehydes gave chalcones **XIIa-c**. In addition to formation of (*E)*-diethyl 8-bromo-4-((4-(1-(2-(2-

cyanoacetyl)hydrazono)ethyl)phenyl)amino) quinoline-3,6-dicarboxylate (**XV)** from its reaction with cyanaceticacidhydrazide **XIV**.

Reaction of diethyl 8- bromo-4-((4-(ethoxycarbonyl)phenyl)amino)quinoline-3,6-dicarboxylate **Xl** with hydrazine hydrate gave the hydrazide derivative **XVII,** which react with 4-nitrobenzaldehyde and ethylisothiocynate giving compounds **XIX** and **XVIII** respectively. O-alkylation of compound **Xh** named as diethyl 8-bromo-4-((4-hydroxyphenyl)amino)quinoline-3,6-dicarboxylate yielded diethyl 8-bromo-4-((4-(2-ethoxy-2-oxoethoxy)phenyl)amino)quinoline-3,6-dicarboxylate(**XX)** which hydrolyzed to a tricarboxylic quinoline compound that named 8-bromo-4-((4-(carboxymethoxy)phenyl)amino)quinoline-3,6-dicarboxylic acid **XXI**.

The structure elucidation of the new compounds was supported by elemental analyses, IR, $^{1}$H NMR, $^{13}$C NMR in addition to mass spectral data.

Also, a brief account on the docking study was explained through the binding conformations in comparison with the cytotoxic results. Additionally, theoretical discussion of biological anticancer and antimicrobial screening was given.

The fourth chapter consists of the experimental part of this work which contains the detailed procedures used for the synthesis of the new starting materials **IIIa-e**, **VIa-c** and **VIIa-d** and the target quinoline compounds **VIII**, **IXa&b**, **Xa-l**, **XIIa-c**, **XV**, **XVII**, **XVIII**, **XIX**, **XX** and **XXI** . In addition, data obtained from the element and spectral analyses as well as their physical properties are given in this chapter. It also sheds the light on the anticancer and antimicrobial activities of most of newly synthesized derivatives compared with doxorubicin and erlotinib as standards cytotoxic agent and gentamicin, cefotaxime , ampicillin , fluconazole and

tioconazole. Compound **XIIa** exhibited the highest cytotoxic activity with $IC_{50}$ 1.88, 3.15 and 1.22 μM against used three cell lines, in addition to compound **XIIc** which showed the highest antimicrobial activity. This chapter also clarifies the correlation between the results of molecular docking and the anticancer activity.