Pharmacological Reports
2011, 63, 305–336
ISSN 1734-1140

Review

Natural and synthetic acridines/acridones as antitumor agents: their biological activities and methods of synthesis

Grzegorz Cholewiński, Krystyna Dzierzbicka, Aleksander M. Kołodziejczyk

Department of Organic Chemistry, Gdansk University of Technology, Narutowicza 11/12, PL 80-233 Gdańsk, Poland

Correspondence: Grzegorz Cholewiński, e-mail: gch@chem.pg.gda.pl

Abstract:
Acridine derivatives constitute a class of compounds that are being intensively studied as potential anticancer drugs. Acridines are well-known for their high cytotoxic activity; however, their clinical application is limited or even excluded because of side effects. Numerous synthetic methods are focused on the preparation of target acridine skeletons or modifications of naturally occurring compounds, such as acridone alkaloids, that exhibit promising anticancer activities. They have been examined *in vitro* and *in vivo* to test their importance for cancer treatment and to establish the mechanism of action at both the molecular and cellular level, which is necessary for the optimization of their properties so that they are suitable in chemotherapy. In this article, we review natural and synthetic acridine/acridone analogs, their application as anticancer drugs and methods for their preparation.

Key words:
acridine/acridone analogs, synthesis, biological activity, anticancer activity

Abbreviations: ABC – ATP-binding cassette protein superfamily, ABCG2 – ATP-binding cassette, sub-family G (WHITE), member 2, CAN – ceric ammonium nitrate, CDI – 1,1'-carbonyldiimidazole, DIPEA – *N,N*-diisopropylethylamine, DMF – *N,N*-dimethylformamide, DMP – Dess-Martin reagent, EDCI – 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride, HOBt – 1-hydroxybenzotriazole, IC_{50} – drug concentration at which 50% inhibition is observed, MDP – *N*-acetyl-muramyl-L-alanyl-D-isoglutamine (muramyl dipeptide), MS – molecular sieves, NAD^+ – nicotinamide adenine dinucleotide, NBS – *N*-bromosuccinimide, NMO – *N*-methylmorpholine *N*-oxide, nor-MDP – *N*-acetyl-nor-muramyl-L-alanyl-D-isoglutamine (nor-muramyl dipeptide), ODNs – oligodeoxynucleotides, PBO – benzoyl peroxide, P-gp – P-glycoprotein, PTSA – *p*-toluenesulfonic acid, TBS – *t*-butyldimethylsilyl, TEBAC – triethylbenzylammonium chloride, TMS – trimethylsilyl, Topo – topoisomerase, TPAP – tetrapropyl ammoniumperruthenate

Introduction

Numerous research groups have focused on the synthesis of new compounds that possess cytotoxic activity, among which acridine/acridone compounds play an important role. Acridine/acridone analogs are known anticancer drugs and cytotoxic agents, and they represent a very interesting class, displaying other forms of bioactivity [7, 20, 39–41, 56, 58, 62, 82]. They are used as biological fluorescent probes, anti-bacterial drugs, e.g., **1–6** [41], anti-protozoal drugs, e.g., **7–12** [20, 39–41, 82], anti-malarial agents, e.g., **13** [6], and anti-HIV drugs, e.g., **14** [40, 53] (Fig. 1).