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This review gives a brief overview on bioactivities of 8-mercaptoquinoline sulfide derivatives involving

antimicrobial activity, anticancer activity, inhibitors as well as other activities. Special emphasis is given to the



# Mini-Review

# Studies on the bioactivities of 8-mercaptoquinoline sulfide derivatives



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Jing-An Zhang <sup>a,b,\*,1</sup>, Li-Jie Zhang <sup>a,b,1</sup>, Xun-Zhong Zou <sup>a,b</sup>, Ya-Jie Liu <sup>a,b</sup>, Wei Gao <sup>a</sup>, Yu Li <sup>c,\*\*</sup>

<sup>a</sup> School of Pharmacy, Guangdong Pharmaceutical University, Guangzhou 510006, People's Republic of China

<sup>b</sup> College of Traditional Chinese Medicine, Guangdong Pharmaceutical University, Guangzhou 510006, People's Republic of China

<sup>c</sup> Department of Environmental Engineering, Guangdong Industry Technical College, Guangzhou 510300, People's Republic of China

# A R T I C L E I N F O

# ABSTRACT

most recent examples.

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#### 1. Introduction

As a simple chemical intermediate, 8-mercaptoquinoline has the vital significance in medical field. To our knowledge, studying the influence of different substituents on 8-mercaptoquinoline can help us to increase the theory of action of organic analytical reagents [1].

Recently, many the structures and properties of 8-mercaptoquinoline and sulfide derivatives have been reported [2–8], not only for the good coordination have abilities, which can be found in Chen et al.'s worked [9–13]; but also for the potential drug values in the field of molecular biology, such as ubiquitin agent inhibitors [14], 11-beta hydroxysteroid

\*\* Corresponding author.

<sup>1</sup> These authors equally contributed to this work.

dehydrogenase type I inhibitor [15], JAMM protein inhibitor [16], potential 5-HT<sub>6</sub> receptor [17], CRTh<sub>2</sub> antagonists [18], Keap1–Nrf2 small-molecule inhibitors [19] and many other enzyme inhibitors [14], anti-mycobacterium tuberculosis [20], pesticides activity [21], and potential application in metal-promoted neurodegenerative diseases [22]. The compound containing 8-quinolinethioether group also can bind to SL3 RNA with higher affinity compare to doubleand single-stranded RNAs that conserved motifs in different strains of HIV-1, which is the decisive factor for viral packaging in Douglas M. Warui's report [23].

The sulfur ether metal complexes containing quinoline group attract our concern for the different physiological activities when metal category and molecular space conformational are changed. This may lead to much stronger DNA-binding performance.

In this review we summarize a number of interesting examples, in which 8-quinolinethioether compounds display various bioactivities, including antimicrobial activity, anticancer activity, inhibitors as well as other activities in medicinal chemistry.

<sup>\*</sup> Correspondence to: J.A. Zhang, School of Pharmacy, Guangdong Pharmaceutical University, Guangzhou 510006, People's Republic of China.

E-mail addresses: zhangja@126.com (J.-A. Zhang), liyuletter@163.com (Y. Li).

### 2. Antimicrobial activities

Our group has been dedicating in the study of the antimicrobial activity of 8-mercaptoquinoline thioether derivatives in the past few years. A series of coordination compounds combined with semi-rigid monothioether and dithioether ligands (Fig. 1): 8-((pyridin-2yl)methylthio) quinoline (1), 8-((pyridin-3-yl)methylthio) quinoline (2), 8-((pyridin-4-yl)methylthio) quinoline (3) and 2,6-bis(8quinolinylthiomethyl) pyridine (4) which contain both quinoline and pyridine terminal groups were obtained. For the position change of substituted group, various coordination modes were also observed [24-30]. Further, the antibacterial and antifungal activities of these coordination compounds were investigated. The results show that most of the compounds have distinct antibacterial activities. As antibacterial agent, these compounds have stronger antibacterial effect for G<sup>+</sup> than G<sup>-</sup>. The antibacterial activity should be mainly attributed to the metal ions with different coordination tendencies and/or positional isomeric effect of pyridine terminal groups from 8-mercaptoquinoline.

However, the antifungal activities of these compounds show that only three compounds having detectable effect to inhibit *fusariumoxysporum f.* sp. cubense.

Chandra et al. [31] designed and synthesized an organic ligand, namely, 8-[{4-(2-substituted phenyl-5-oxo-thiazolidin-1-yl)-5thiobutyl triazolo} methoxy] quinolines, which is the derivative of 8substituted quinolone containing 1,2,4-triazole and thiazolidinone groups. The antibacterial effect was evaluated in vitro through diffusion method. The compounds are against some pathogenic strains. When a p-lactam moiety was incorporated to the 8-substituted quinolone, the antibacterial have been improved. 3-substituedaryl-[2'-methyl-2'-ohydroxyphenyl-5'-oxo-thiazolidin-1'-yl]-5-thio-quinolin-8'-yl-(1,2,4)triazoles (**5**) (Fig. 2) was to proven a potent antifungal against *Candida albicans*, and the effect was similar to the standard drug of fluconazole.

# 3. Anticancer activity

With the change of people's living habits and environment, cancer has been the first killer for human health in the world.

Recently, some pharmaceutical contains 8-thio (mercapto) quinoline or quinazoline ring was found to have special effect for the treatment of neoplastic maladies and other abnormal non-differentiated cells.

Zhou et al. [16,32,33] synthesized a series of 8-thio quinolinethiol derivatives used for JAMM protein inhibitors (Fig. 3). To identify the

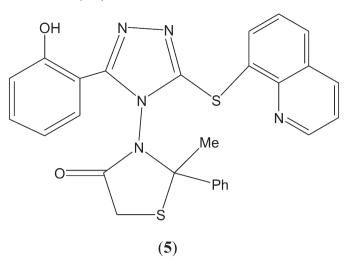


Fig. 2. The structure of compound 5.

bioactivities of these compounds, Rpn II biochemical assay and a Csn5 assay were used. It shows that all the compounds have inhibitory activities for  $IC_{50}$  in the Rpn II assay, which indicates the favorable inhibitory activities from these quinoline compounds in vivo.

Now extensive research has been focused on metallopharmaceuticals for the discovery of anti-cancer activities of *cis*-platin [34, 35]. In addition to platinum, other metal complexes, such as gold [36] and ruthenium [37], also have promising anti-cancer effect.

Recently, a number of Osmium(II) arene complexes have been found to display anticancer activities in vitro [38].

Tang et al. [39,40] investigated the cytotoxicity of nine nitride osmium complexes containing 8-quinolinolato group (Fig. 4), towards four human cancer cell lines, including cervical epithelioid carcinoma (HeLa), liver hepatocellular carcinoma (HepG2), colorectal carcinoma (HCT 116) and lung carcinoma epithelial 6 (A549) by the way of MTT assays. All complexes have obvious cytotoxic effects towards cancer cells. However, the neutral complexes (**6**–**9**) display much higher efficiencies for cellular uptake and cytotoxicity than the anionic complexes (**11–14**). The Os<sup>VI</sup> = RN was proven promising in preparing high-valent anti-cancer drugs.

In addition, the quinoline and 1,2,3,4-tetrahydroquinoline groups are often used to design diverse anticancer drugs. When brominated

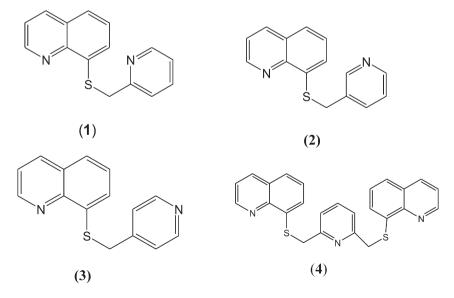


Fig. 1. The structure of compounds 1-4.

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