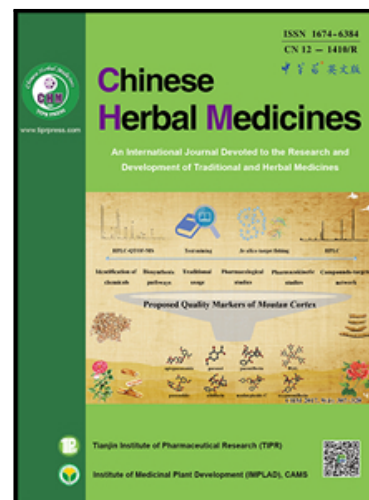


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Synthesis and Biological Evaluation of New Peroxo-bridged Diosgenin Derivatives

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ABSTRACT

Objective In order to find lead compound with anti-HBV activity from peroxo-bridged diosgenin derivatives obtained with Eosin Y as the photosensitizer. **Method** Eosin Y was used as the photosensitizer to activate the oxygen in the air to synthesize novel diosgenin derivatives with peroxo-bridge. The structures of synthesized compounds were identified by NMR and HR-MS. Their cytotoxicity and anti-hepatitis B activity were evaluated *via* MTS assay and ELISA method, respectively. **Results** Six diosgenin derivatives were synthesized, three of which contain peroxo-bridge, and their structures were confirmed by spectroscopy. It showed that 5 α ,8 α -peroxo-6-alkenyl-diosgenin(7) could suppress the production of HBsAg on transfected HepG2.2.15 cells at low-toxic concentration and the inhibition rate (%) on HepG2.2.15 cells was 18.28% at 12.50 μ g/mL, better than that of 3TC (7.30% at 12.50 μ g/mL) and others. **Conclusion** Due to its lower cytotoxicity and potential anti-hepatitis B activity, compound 7 could be developed as the promising candidate of anti-hepatitis B drug. It also indicated that the peroxo-bridged derivatives had potential biological values for developing clinical agents.

Keywords peroxo-bridged derivatives; diosgenin; Eosin Y; anti-hepatitis B

1. Introduction

It was reported that some compounds with peroxo-bridge show remarkable biological activities. Artemisinin, for which Youyou Tu won the Nobel Prize in physiology or medicine in 2015, had been applied as clinical antimalarial agent for its peroxo-bridged structure (Dechy-Cabaret et al, 2000; Miller et al, 2011). Metal complexes with peroxo-bridge might have potential activities, such as antifungal, antiparasitic, anti-helicobacter pylori infection, and so on (Miller et al, 2011; Anitha et al, 2012; André-Barrès et al, 2005; Goswami et al, 2012). In our previous work, some steroid compounds with peroxo-bridge had been isolated from *Styela clava* Herdman (Cai et al, 2003) and demonstrated promising anti-hepatitis B virus activity (anti-HBV) (Cai et al, 2003; 2006). In view of the low content in natural plant kingdom and potential bioactivity advantages, the novel peroxo-bridged derivatives need to be designed and synthesized. Diosgenin, the steroid compound isolated from many Chinese herbal medicines and plants, had exhibited a wide range of health beneficial properties, such as anti-inflammatory, antiapoptotic, antihyperglycemia, anticancer, antidiabetes, antihypercholesterolemia, and hepatoprotective activities (He et al, 2012; Li et al, 2010; Srinivasan et al, 2009; Chen et al, 2016; Kalailingam et al, 2014; Fuller et al, 2015). Thus, diosgenin had a great value for further synthetic modifications to develop potential agents. In this study, some novel diosgenin derivatives with peroxo-bridge were designed and synthesized.

The peroxo-bridged derivatives were mainly synthesized by oxidants, such as bromine/hydrogen peroxide and metal complexes/hydrogen peroxide (Chrappová et al, 2009; Wang et al, 2012; Haldar et al, 2011; Tabneret al, 2001). Usually, these reagents were special and expensive, and it needs harsh conditions to synthesize the peroxo-bridged structure. The catalytic oxidation of photosensitizer had been reported for a long time. In 1931, Kautsky discovered dye-sensitized photo-oxygenations *via* singlet oxygen (Kautsky et al, 1931). In 1964, Wexler and Taylor proved that dye-sensitized photo-oxygenations were similar to that of chemically generated singlet oxygen (Foote et al, 1964; Corey et al, 1964). In our previous study, Eosin Y had been used as the photosensitizer to catalyze epoxy ring in the structure of oleanolic acid, and peroxo-bridge in cholesterol and β -sitosterol (Yan et al, 2016; Jia et al, 2017). In our present study, the conjugated dienes

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