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Selected organophosphorus compounds with biological activity. Applications in medicine

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The purpose of this article is to provide an overview of the latest applications of organophosphorus compounds (OPs) that exhibit biological activity. A large family of OPs have become popular in recent years. The practical application of OPs in modern medicine has been attributed to their unique properties. In this article, the methods used to select these compounds will be emphasized. This paper will first outline the findings of a literature review on OPs, including anticancer and antiviral agents, bisphosphonates, phosphorus analogues of amino acids and peptides, and organophosphorus metal complexes, and secondly, it will classify the compounds according to their biological activity and applications in the treatment of diseases.

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1. Introduction

Organophosphorus compounds (OPs), which are a wide class of chemical compounds containing organic moieties usually bonded directly to phosphorus or bonded through a heteroatom, such as sulfur, oxygen or nitrogen, are some of the most common chemicals in the human environment. Because of their unique properties and high biological activity, they have largely been used worldwide in agricultural (pesticides),¹ industrial (production of lubricants, hydraulic fluids, and plastics materials),² medicinal (drugs against osteoporosis, anticancer and antiviral compounds)^{3,4} or veterinary (anthelmintics) applications.⁵ The first potent synthetic organophosphorus poison, tetraethyl pyrophosphate (TEPP), was synthesized by Clermont in 1854. At the beginning of the twentieth century, some very toxic compounds were used in many armed conflicts as chemical weapons, known as chemical warfare agents (CWA). Following the German laboratories discovery of soman, sarin and tabun, the United States and England developed VX production technologies. The book “Chemical Warfare Agents”⁶ discusses the physicochemical properties of chemical warfare agents, their dispersion and fate in the environment, their toxicology and management of their effects on humans, decontamination, and protective equipment. After the Second World War, OPs have been used mainly as pesticides for plants and animals. Furthermore, OPs have practically contributed to the substantial benefits for efficient food production and the fight against many serious diseases, such as malaria, yellow fever, typhus,⁷ or smallpox.⁴

2. Bisphosphonates in the treatment of osteoporosis

Osteoporosis is one of the most serious health problems in the world, and prevention and treatment are of great interest in the European Union, which issued “Report on Osteoporosis in the European Community – Action for Prevention”.⁸ The scale of the problem is alarming. One in three women and one in eight men over the age of 50 years will experience at least one fracture due to osteoporosis in their lifetime. The main criterion for selecting an osteoporosis therapy is its impact on the risk of osteoporotic fracture (femoral neck, spine, wrist). The following pharmacological methods are used:

- hormone replacement therapy;
- specific estrogen receptor modulators (SERMs);
- calcitonin;
- vitamin D3 with active metabolites and calcium;
- fluorine.

Bisphosphonates are currently the most important and effective class of drugs developed for the treatment of metabolic bone disorders associated with increased osteoclast-mediated bone resorption, such as osteoporosis^{9,10} and Paget's disease.^{11,12} They are effective inhibitors of tumor-induced bone destruction and significantly reduce the incidence of skeletal complications in patients with bone metastases from several forms of cancer, including breast and prostate cancer.¹³ Bisphosphonates have a high affinity for calcium and therefore specifically target bone mineral, where they are internalized by bone-destroying osteoclasts and inhibit their function.¹⁴ Importantly, potential of bisphosphonates has also been identified in areas ranging from parasite-growth inhibition to immunological and cancer therapeutics.³ These compounds primarily affect the function of osteoclasts, but recent preclinical evidence indicates that other neighboring cell types, such as

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