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# COMPUTATIONAL INVESTIGATION OF PESTICIDE INDUCED OXIDATIVE STRESS AND ITS IMPACT ON THE CHRONIC KIDNEY DISEASE OF UNKNOWN ETIOLOGY (CKDU)

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**Abstract:** The chronic kidney disease of unknown etiology (CKDu) has been a major health issue in Sri Lanka within the last three decades. Many investigative efforts have been carried out to identify its unknown origin and several risk factors which have been associated. A possible link between oxidative stress and the progression of the disease has been identified. The environmental factors which favor the development of oxidative stress are prevalent in those affected areas. The study of "pesticide induced oxidative stress" has been a topic of research interest. Alterations in the balance between the production of free radicals and the antioxidant defenses were recognized as one of the main causes. Four major pesticides were docked with different enzymes which directly related to mechanisms in generating oxidative stress, using Auto Dock molecular docking program. The strength of the binding of the pesticide in the binding site of the corresponding enzyme was used to emphasize its potential interaction with Cytochrome P450 A34enzyme. According to molecular docking investigations, it was evident that three organophospahates; Profenofos, Diazinon and Chlrofyrifos possessed relatively similar binding energies at the active site compared to the inducer for Cytochrome P450 A34 enzyme. These organophosphates behave as the potent enzyme inducers as well as substrates which involved in bio-activation. The computational findings directed to disclose how reactive oxygen species were generated to cause oxidative stress and it can be utilized to predict mechanistic steps related to the pesticide induced oxidative stress.
**Keywords:** CKDu, oxidative stress, organophosphates, cytochrome P450.

## INTRODUCTION

Chronic Kidney Disease (CKD) is the loss of kidney function over a period of time. It is a global health problem where diabetes, hypertension, and the various forms of glomerulonephritis are well-recognized etiologies [1]. The disease is said to be "chronic" because it takes many years for symptoms to develop. The etiology is uncertain to the date; hence the disease is known as the Chronic Kidney Disease of uncertain etiology (CKDu). This has been reported in Sri Lanka, several Central American countries, Andhra Pradesh in India and the El-Minia Governorate in Egypt [2]. The disease is characterized by substantial morbidity and mortality, resulting in death of adult patients. Progression of CKDu is

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