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Cannabinoid Receptor 1 Inhibition in Chronic Kidney Disease: A New Therapeutic Toolbox

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Chronic kidney disease (CKD) concerns millions of individuals worldwide, with few therapeutic strategies available to date. Recent evidence suggests that the endocannabinoid system (ECS) could be a new therapeutic target to prevent CKD. ECS combines receptors, cannabinoid receptor type 1 (CB1R) and type 2 (CB2R), and ligands. The most prominent receptor within the kidney is CB1R, its endogenous local ligands being anandamide and 2-arachidonoylglycerol. Therefore, the present review focuses on the therapeutic potential of CB1R and not CB2R. In the normal kidney, CB1R is expressed in many cell types, especially in the vasculature where it contributes to the regulation of renal hemodynamics. CB1R could also participate to water and sodium balance and to blood pressure regulation but its precise role remains to decipher. CB1R promotes renal fibrosis in both metabolic and non-metabolic nephropathies. In metabolic syndrome, obesity and diabetes, CB1R inhibition not only improves metabolic parameters, but also exerts a direct role in preventing renal fibrosis. In non-metabolic nephropathies, its inhibition reduces the development of renal fibrosis. There is a growing interest of the industry to develop new CB1R antagonists without central nervous side-effects. Experimental data on renal fibrosis are encouraging and some molecules are currently under early-stage clinical phases (phases I and IIa studies). In the present review, we will first describe the role of the endocannabinoid receptors, especially CB1R, in renal physiology. We will next explore the role of endocannabinoid receptors in both metabolic and non-metabolic CKD and renal fibrosis. Finally, we will discuss the therapeutic potential of CB1R inhibition using the new pharmacological approaches. Overall, the new pharmacological blockers of CB1R could provide an additional therapeutic toolbox in the management of CKD and renal fibrosis from both metabolic and non-metabolic origin.

Keywords: cannabinoid, cannabinoid receptor type 1, chronic kidney disease, endocannabinoids, renal fibrosis

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