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Original

Reno-protective effects of propolis on gentamicin-induced acute renal toxicity in swiss albino mice

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ABSTRACT

Background: Kidney is a vital organ which plays an important and irreplaceable role in detoxification and removal of xenobiotics. And therefore is vulnerable to develop various forms of injuries. Hence, making it immensely important to search for natural reno-protective compounds.

Objectives: This study therefore, aims to evaluate the reno-protective properties of propolis against gentamicin induced renal toxicity in mice.

Methods: Three groups of 10 male mice each were used for this study. First group served as control, the second group (Gm group) was administered orally 80 mg/kg body weight gentamicin for 7 days, and the third group (GmP group) was administered same dose of gentamicin with propolis (500 mg/kg body weight) for 7 days. Various parameters were used to study the renal toxicity.

Results: Gentamicin caused significant renal damage as evident by the rise in BUN levels, diminished glomeruli hypocellularity, moderately dilated tubules, and mild loss of brush border, severe infiltration, extensive tubular degeneration and presence of tubular cast. Histochemistry results show presence of collagen and reticular fibres. Immunohistochemical reactions show kidney injury (Kim-1 gene-expression), oxidative stress (MDA gene-expression), and an increase in apoptosis (caspase-3 gene-expression). Co-administration of propolis with gentamicin showed significant decrease in BUN levels, appearance of healthy glomeruli with normal cellularity, reduction of tubular injury, decrease of collagen and reticular fibres deposition, reduction of apoptosis, kidney injury and oxidative stress.

Conclusion: Results presented in this study clearly show the reno-protective role of propolis against gentamicin-induced toxicity on mice kidney.

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Efectos renoprotectores del propóleo sobre la toxicidad renal aguda inducida por gentamicina en ratones albinos suizos

Palabras clave:
Gentamicina
Propóleo
Riñón
Apoptosis
Estrés oxidativo

RESUMEN

Antecedentes: El riñón es un órgano vital que desempeña una función importante e insustituible en la desintoxicación y la eliminación de los xenobióticos y, por lo tanto, es vulnerable a desarrollar diversas formas de lesión. Esto hace muy importante la búsqueda de compuestos renoprotectores naturales.

Objetivos: Este estudio tiene como objetivo evaluar las propiedades renoprotectoras del propóleo contra la toxicidad renal inducida por gentamicina en ratones.

Métodos: Para este estudio se utilizaron 3 grupos de 10 ratones macho en cada uno. El primer grupo sirvió como control, el segundo grupo (grupo Gm) recibió 80 mg/kg de peso corporal de gentamicina por vía oral durante 7 días y el tercer grupo (grupo GmP) recibió la misma dosis de gentamicina con propóleo (500 mg/kg de peso corporal) durante 7 días. Se utilizaron varios parámetros para estudiar la toxicidad renal.

Resultados: La gentamicina causó daño renal significativo, como demostró el aumento de los niveles de nitrógeno ureico en sangre, la disminución de la hipocelularidad glomerular, los túbulos moderadamente dilatados y la pérdida leve del borde en cepillo, la infiltración grave, la degeneración tubular extensa y la presencia de cilindros tubulares. Los resultados de la histoquímica muestran presencia de colágeno y fibras reticulares. Las reacciones inmunohistoquímicas muestran lesión renal (expresión del gen Kim-1), estrés oxidativo (expresión del gen MDA) y un aumento de la apoptosis (expresión del gen caspasa-3). La administración concomitante de propóleo con gentamicina mostró disminución significativa de los niveles de nitrógeno ureico en la sangre, aspecto de glomérulos sanos con celularidad normal, reducción de la lesión tubular, disminución de colágeno y deposición de fibras reticulares, reducción de la apoptosis, daño renal y estrés oxidativo.

Conclusión: Los resultados presentados en este estudio muestran claramente la función renoprotectora del propóleo contra la toxicidad inducida por gentamicina en el riñón de los ratones.

Introduction

Gentamicin is commonly used aminoglycoside antibiotic for the treatment of various bacterial infections. The recommended routes of administration of gentamicin are intravenous, intramuscular, intraperitoneal or topical as it is not sufficiently absorbed by the intestinal tract.[1,2] However, potential clinical use of gentamicin is limited due to gentamicin-induced toxicity, even at doses slightly higher than recommended doses. Gentamicin can cause tissue injury such as nephrotoxicity, ototoxicity[3,4] and liver toxicity,[5] possibly through generation of free oxygen radicals. Nephrotoxicity of gentamicin arises due to its accumulation in renal cortical tubular epithelial cells.[2] Although the pathogenesis of gentamicin-induced acute kidney injury (AKI) has been the focus of a large number of studies, the underlying mechanisms are not yet fully elucidated. Recent studies suggest that gentamicin nephrotoxicity is a complex and multifaceted process in which gentamicin triggers cellular responses involving multiple pathways that culminate in renal damage and necrosis.[6,7] Therefore, a number of different molecular markers are being used to assess the kidney injury including Kidney Injury Molecule-1 (KIM-1), markers for apoptosis and oxidative stress.[8–10]

Several agents and strategies have been attempted to ameliorate gentamicin nephrotoxicity[11–13] with main focus on the use of various antioxidant agents including the extracts from medicinal plants with antioxidant properties.[11] However, none of these have been found safe/suitable for clinical practice due to known and unexplored side effects. Propolis a gum like substance gathered by bees from various plants and varies in colour from light yellow to dark brown,[14] possesses a broad spectrum of biological activities such as anti-hepatitis and anti-arthritis, and is also known to enhance immune system.[15–17] This biological activity may be attributed to its constituents obtained from plants, mainly phenolic compounds such as flavonoids. Flavonoids are well-known antioxidant possessing free radical scavenging and metal chelating activity.[18] At least 38 different flavonoids have been reported in propolis.[19] Some components of the propolis are absorbed and circulate in the blood and behave as hydrophilic antioxidant and save vitamin C.[20] The present study therefore evaluates the potential of propolis when administered orally to protect the kidney against the harmful effects and acute nephrotoxicity of gentamicin in swiss albino mice.

Materials and methods

Animals

Swiss albino male mice weighing 25± g were used for the experiment. These animals were acclimated to 22 ± 1 °C and