

## Synthesis of Resveratrol Loaded mPEG-PLA Nanomicelles for the Prevention of Osteoporosis in Ovariectomized Rats

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**SUMMARY.** Resveratrol loaded mPEG-PLA co-polymeric nanomicelles were synthesized using dialysis membrane technique and their osteoporosis preventive ability in ovariectomized Sprague-Dawley female rats was studied. Results showed that the synthesized nanomicelles were  $52.87 \pm 3.8$  nm in diameter and had drug loading and encapsulation efficiency of  $11 \pm 2.3\%$  and  $72.8 \pm 2.4\%$ , respectively. This formulation further exhibited biphasic sustained release of resveratrol over a long period of time. In addition, increased bioavailability of resveratrol was elucidated in its nanomicellar formulation as compared to free resveratrol in rats. The synthesized resveratrol based nanomicelles significantly increased both bone mineral density and bone strength at equivalent dose of free resveratrol. The increased restoration of bone turnover markers (osteocalcin and C-terminal teleopeptide of type 1 collagen) was also revealed. The oral administration of mPEG-PLA-Res nanomicelles displayed more prominent protective effect on osteoporosis in an ovariectomized rat model in comparison to free resveratrol treatment.

**RESUMEN.** Se sintetizaron nanomicelas copoliméricas mPEG-PLA cargadas con resveratrol usando la técnica de membrana de diálisis y se estudió su capacidad preventiva de osteoporosis en ratas Sprague-Dawley ovariectomizadas. Los resultados mostraron que las nanomicelas sintetizadas eran de  $52,87 \pm 3,8$  nm de diámetro y tenían una carga de fármaco y eficiencia de encapsulación de  $11 \pm 2,3\%$  y  $72,8 \pm 2,4\%$ , respectivamente. Esta formulación mostró además una liberación bifásica sostenida de resveratrol durante un largo periodo de tiempo. Además, el aumento de la biodisponibilidad del resveratrol se elucidó en su formulación nanomicelar en comparación con el resveratrol libre en ratas. Las nanomicelas sintetizadas en base a resveratrol aumentaron significativamente la densidad mineral ósea y la resistencia ósea a una dosis equivalente de resveratrol libre. También se reveló el aumento de la restauración de los marcadores de rotación ósea (osteocalcina y teleopéptido C-terminal de colágeno tipo 1). La administración oral de nanomicelas de mPEG-PLA-Res mostró un efecto protector más prominente sobre la osteoporosis en un modelo de rata ovariectomizado en comparación con el tratamiento con resveratrol libre.

**KEY WORDS:** bone mineral density, mPEG-PLA, nanomicelles, osteoporosis, resveratrol,

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