

ABSTRACT

*Bone cancer is a rare disease with a global survival rate of about 68%. Conventional treatment has limitations, including the risk of recurrence and side effects. Therefore, scaffolds-based implants have the potential to improve bone regeneration and prevent cancer cell recurrence. Chitosan and gelatin, as the main ingredients of scaffolds, have biocompatibility and biodegradability, but the risk of inflammation and bacterial infection remains a challenge. Antioxidant-rich betel leaf extract (*Piper betle* L.) was added to chitosan-gelatin scaffolds to reduce inflammation and enhance antitumour activity. *Piper betle* L. extract was obtained through maceration with 90% ethanol at a ratio of 10% w/v, followed by phenol and flavonoid content testing. Fabrication of scaffolds was carried out by varying chitosan (2%, 4%, 6%, 8% w/v) and gelatin 2% w/v (2:3 v/v ratio), using glutaraldehyde 0.1% v/v, and *Piper betle* L. extract 9% w/v. Fabrication was done by freeze-drying method, and characterisation included FTIR, degradation, swelling, and antibacterial tests. The results showed that the phenol content (64.36 mg/g) was higher than flavonoids (37.15 mg/g). FTIR analysis confirmed stable molecular interactions through increased hydrogen bonding at the hydroxyl group (-OH) at 3500-3200 cm^{-1} as chitosan concentration increased. The degradation rate was faster in the high porosity scaffolds: K2G-PB9 (14%) and K4G-PB9 (11%), compared to K6G-PB9 (9%) and K8G-PB9 (5%) which are more structurally stable. The highest swelling ratio was found in K2G-PB9 (201%), followed by K4G-PB9 (151%), K6G-PB9 (107%), and K8G-PB9 (101%). Antibacterial activity increased as the chitosan increased, with the highest zone of inhibition in K8G-PB9 against *S. aureus* (12.28 mm) and *E. coli* (11.24 mm). The K8G-PB9 scaffolds showed stable structural stability, optimal degradation and swelling values, and good antibacterial activity, thus meeting the standards as implant candidates for bone cancer therapy.*

Keywords: *Bone cancer, Chitosan, Gelatin, Inflammation, *Piper betle* L. extract., Scaffolds*