ABSTRACT

Nanotechnology is the most dynamic area of research in recent materials science creating an impression in all domains of human life. There is amplified call of nanoparticles because of their wide-ranging applications in numerous zones such as medicine, electronics and environmental sciences. Nanotechnology linking phytofabrication of nanoparticles has developed an attention-grabbing clue and has gained much prominence and significance in current ages. Nanotechnology has unlocked a new site in the improvement of nanomedicine. Fabrication of noble metal nanoparticles has been concerned ample attention due to their potential uses. In current investigation silver nanoparticles (AgNPs) from *Berberis lyceum* Royle (Royle, 1837) root bark (BLR) extract were synthesized, characterized and analyzed for different therapeutic activities. Synthesis was confirmed by UV-spectroscopy and then BLR AgNPs were characterized by different techniques such as Scanning Electron Microscopy (SEM), Transmission Electron Microscopy (TEM), Fourier Transform Infrared Spectroscopy (FTIR) and X-ray Differaction (XRD). Morphological studies exposed that fabricated BLR-AgNPs were mostly spherical in shape and average size was 18 nanometers. These bioengineered AgNPs and extract was analyzed for antibacterial, antioxidant, antidiabetic, anticancerous, hepatoprotective and wound healing activity. From current study, it was observed that BLR-AgNPs were greatly effective against tested bacteria. BLR-AgNPs revealed highest activity against *Streptococcus pyogenes* (16.7±0.3 mm). The lowest antibacterial activity was reported against *Escherichia coli* (1.1±0.1 mm). In case of minimum inhibitory concentration it was observed that BLR-AgNPs with 10 µg/mL concentrations showed highest activity while 2.5 µg/ml BLR-AgNPs showed least inhibitory activity.

In vitro antioxidant activity of BLR extract and BLR AgNPs was measured. It was measured by 2,2-diphenyl-1-picrylhydrazyl (DPPH) free radical scavenging method. Antioxidant activity of 20 µg/mL, 40 µg/mL, 60 µg/mL, 80 µg/mL and 100 µg/mL of BLR extract and BLR AgNPs was measured. When the concentration of BLR extract and BLR AgNPs rose from 20 µg/mL to 100 µg/ml, the antioxidant activity raised from 10.5±0.29% to 44.8±0.6% and 17±0.58% to 62±1% respectively. The highest antioxidant activity was recorded as 62±1% with 100 µg/mL treatment with BLR AgNPs.

In vitro and *in vivo* antidiabetic activity was analyzed. BLR-AgNPs showed greater *in vitro* and *in vivo* antidiabetic activity as compared to BLR-extract. In case of *in vivo* activity blood glucose level was checked at seven day interval for 28 days. At the end of experimental period different biochemical, hematological and histological parameters were studied. Glucose level dropped to 128±2.7 mg/dL when treated with BLR extract and BLR AgNPs dropped this level to 116.5±5.09 mg/dL as compared to diabetic group (333.75±33.5 mg/dL). For the appraisal of lipid profile, concentrations of triglycerides, total cholesterol, high-density lipoprotein cholesterol (HDL-C), low-density lipoprotein cholesterol (LDL-C) and very low-density lipoprotein cholesterol (VLDL-C) were measured. Upsurge in triglycerides, total cholesterol, LDL-C and VLDL-C and decline in HDL-C was seen in alloxan induced diabetic mice. Mice of therapeutic groups treated with extract and AgNPs have exposed noteworthy reduction in above mentioned serum factors except HDL-C which was increased after treatment. Level of alanine aminotransferase (ALAT), aspartate transaminase (AST), alkaline phosphatase (ALP), bilirubin and lipid peroxidation (LPO) increased while that of total protein, catalase (CAT) and superoxide dismutase (SOD) decreased in diabetic mice but these hepatic markers were sustained in their normal range in extract and AgNPs treated mice. Changes in renal function tests (RFTs) were also seen in current experiment. Urea, uric acid and creatinine level was increased and albumin level was decreased in diabetic mice. These changes were significantly reversed after treatment with BLR extract and AgNPs. The total white blood cells (WBCs) count, neutrophils, hematocrit and platelets displayed a significant proliferation while lymphocytes, haemoglobin (Hb), mean corpuscular volume (MCV) and red blood cells (RBC) count declined in diabetic mice group. These changes were normalized after treatment with BLR extract and AgNPs. No significant change was seen in other hematological parameters. Histological study of liver, kidney and pancreas also showed the antidiabetic effect of BLR.

In vitro and *in vivo* anticancerous study showed the anticancerous potential of BLR. For anticancerous study different parameters such as alanine aminotransferase (ALAT), aspartate transaminase (AST), alkaline phosphatase (ALP), lactate dehydrogenase (LDH), alpha-feto protein (AFP), gamma-glutamyl transferase (γ -GT), 5 nucleotidase (5NT), glucose-6-phosphate dehydrogenase (G6PDH),

bilirubin and albumin were studied. All parameters showed increased level in diethyl nitrosamine (DEN) treated mice except albumin that was decreased. All changes were significantly reversed after BLR extract and BLR AgNPs treatment.

For the sake of hepatoprotective potential of BLR parameters like ALAT, ASAT, ALP, LDH, bilirubin, total protein, malondialdehyde (MDA), glutathione (GSH) and CAT were analyzed. ALAT, ASAT, ALP, LDH, bilirubin, and MDA level displayed significant increase while total protein, GSH and CAT level decreased in CCl_4 treated mice. All changes were significantly reversed by BLR AgNPs and only few changes were significantly reversed by BLR extract. Histological study of liver also showed the hepatoprotective effect of BLR.

Wound healing activity results showed that BLR extract and AgNPs have wound healing capacity. BLR AgNPs showed more activity (0.06±0.02 cm) than BLR extract (0.46±0.02 cm) in wound size as compared to wounded (1.1±0.06 cm). Hematological parameters of wounded and treated group were also studied. All parameters showed no significant changes except WBCs, RBCs and platelets. WBCs (6.43±0.41 $10^3/\mu L$) and platelets (574.3±6.8910$^3/\mu L$) increased while RBCs (3.32±0.20 $10^6/\mu L$) level decreased in untreated mice. Level of WBCs, RBCs and platelets was normalized in BLR extract (4.33±0.09 $10^3/\mu L$; 5.17±0.07 $10^6/\mu L$, 341.3±32.49 $10^3/\mu L$) and BLR AgNPs (4.13±0.32 $10^3/\mu L$; 5.23±0.19 $10^6/\mu L$; 279.33±26.7 $10^3/\mu L$) treated mice. Current study investigated that BLR extract and its green synthesized silver nanoparticles have great potential in treating different diseases.