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Investigation on effect of basalin coated silver nanoparticles as antioxidant for alleviating peripheral neuropathy in mice treated with oxaliplatin

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ABSTRACT

A facile, convenient, and green method for the synthesis of BAgNPs by using basalin is proposed in this work. The capping of the basalin on the surface of BAgNP was confirmed by the zeta potential and FTIR findings. Further, we have injected prepared BAgNPs into oxaliplatin-treated mice to alleviate neuropathic pain. The aluminum levels in the DRG were reduced by the chelating activity of BAgNPs. Moreover, behavioral analyses also manifested that the accumulation of aluminum on the DRG might be a reason for neuropathic hyperalgesia. These findings also recommended that the chelation of aluminum by AgNPs could provide an effective remedy to alleviate the symptoms of oxaliplatin-induced neuropathic pain in cancer patients.

1. Introduction

Oxaliplatin is diaminocyclohexane platinum alkylating agent which is specially employed in the treatment of advanced colorectal or bowel carcinoma [1]. Majority of patients undergoing chemotherapy with oxaliplatin suffer from peripheral neurotoxicity [2]. In particular, the toxicity is brought about by the inhibition of duplication of DNA in the metastatic cells [3]. This drug hinders the process of DNA replication and transcription by developing cross links in DNA, thus resulting in cell apoptosis [4]. Peripheral neuropathy is mostly associated with reversible tingling and numbness, hypersensitivity to colder temperatures, and intense pain associated with cramping of both hands and feet [5,6]. Peripheral neuropathy stimulated by oxaliplatin can be categorized into acute type, which is typified by cold hyperalgesia precisely following the treatment, and the other being chronic type, which induces irreversible neuronal impairment triggered by constant medication.

Acute neuropathic syndrome is resulted from the calcium chelation by oxalate released from oxaliplatin that affect the neural inflammation [7]. In contrary, chronic neuropathy is caused by the deposition of heavy metals like platinum in dorsal root ganglion cells [8]. Some of the common drugs employed in the treatment of peripheral neuropathy comprise of analgesics, antidepressants, anticonvulsants, dietary supplements, and local anesthetics, although these scarcely lessen the symptoms to certain level despite of the definite mechanism of neuropathy [9]. From the recent survey, it is evident that administration of antioxidants like alpha-lipoic acid or vitamin C and acetyl-L-carnitine could ease the symptoms of oxaliplatin-induced hyperalgesia [10], indicating the crucial role of oxidative stress in pain induced by peripheral neuropathy. In addition, Ca-Mg combinations and other neuromodulatory agents have been routinely employed as therapeutic elements however they are not entirely successful in relieving the pain [11]. Vitamin-E is an antioxidant that has the ability to detoxify the ROS membranes and synapses [12].

In the earth's crust, aluminum (Al) is the most abundant metallic element and also in our food stuff along with drinking water sources but not a vital element in our diet. In turn, bioaccumulation of Al results in neurotoxicity and other health problems like dialysis encephalopathy syndrome and osteomalacia [13,14]. Al induces organ toxicities affecting the, bones, kidneys, blood, brain, and nervous system [15]. Although, there is an escalating rise of awareness about the bioaccumulation of Al contact would result in neurotoxicity, yet the action mechanism of Al toxicity remained vague and unexplained.

Transient Receptor Potential Ankyrin-1 (TRPA1) also renowned as capsaicin receptor is a protein that is triggered by dreadful physical or chemical stimuli, by adverse heat (at 42 °C), and produced by oxaliplatin, thus could help in preventing neurotoxin effect of the drug [16]. Localization of TRPA1 is prominent in sensory neurons of the dorsal root ganglia (DRG) [17]. In order to study this observation, oxaliplatin treated mice were tested for consequent stimulation of cold hyperalgesia by behavioral tests. Inductively coupled plasma mass spectrometry (ICP-MS) was used to test the accumulation of metals in the DRG and real-time PCR and immunological staining methods for analyzing the expression of TRPA1.

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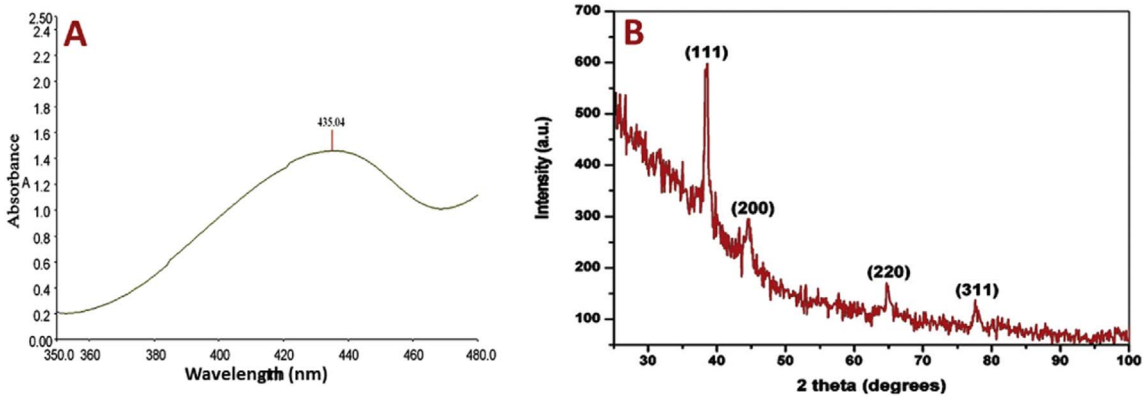

Fig. 1. UV–visible absorption (A) and XRD pattern (B) of silver nanocolloid.

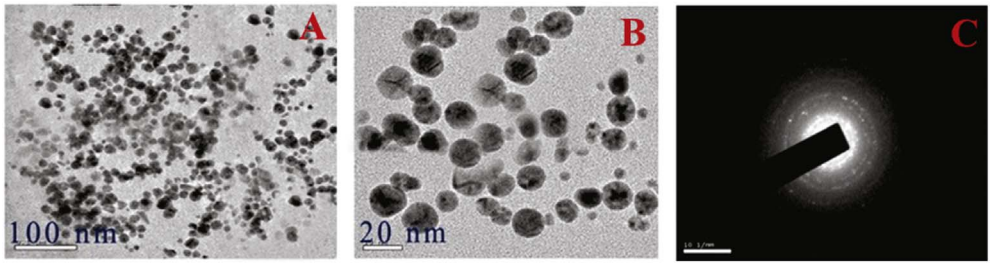

Fig. 2. TEM images (A, B), SAED pattern (C) of the BAgNPs.

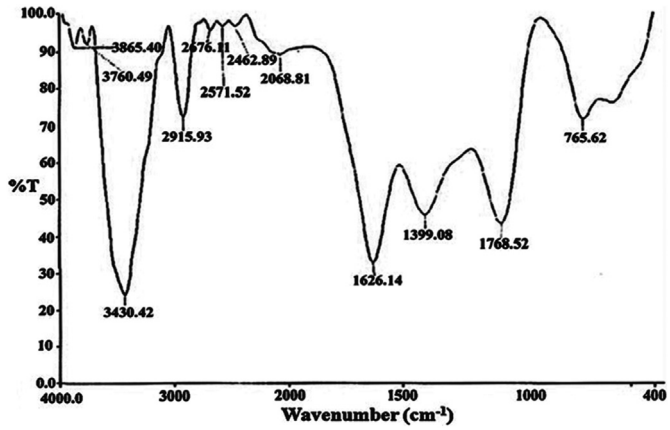

Fig. 3. FTIR spectrum of biosynthesized BAgNPs.

On the other hand, the biofabricated nanoparticles are of significant scientific interest in course of their potentially advanced applications in various disciplines of medicine [18]. The bio-fabrication of nanoparticles using polyphenols of plant origin, microorganisms and biomolecules could be considered as best methods to produce biocompatible material to use in biological applications [19]. From a recent survey, it was evident that various bio-reagents such as, amino acids [20], proteins [21], and plant extracts were being used for the green synthesis of nanoparticles. In vein, the significant properties of AgNPs were crucially dependent on the crystalline structure, size, shape, and surface functionalities of the nanoparticles [22]. Therefore, there is an essential requisite for the advancement of new AgNPs synthesized from green approach for potential applications in nanomedicine and biology.

In the present work, we have demonstrated a fast and facile technique of basalin coated AgNPs synthesis in aqueous medium using silver nitrate ($AgNO_3$). We have further studied the impact of basalin coated silver nanoparticles on oxaliplatin-induced peripheral neuropathic symptoms by means of aluminum accumulation and TRPA1 expression in the dorsal root ganglion in oxaliplatin treated mice.

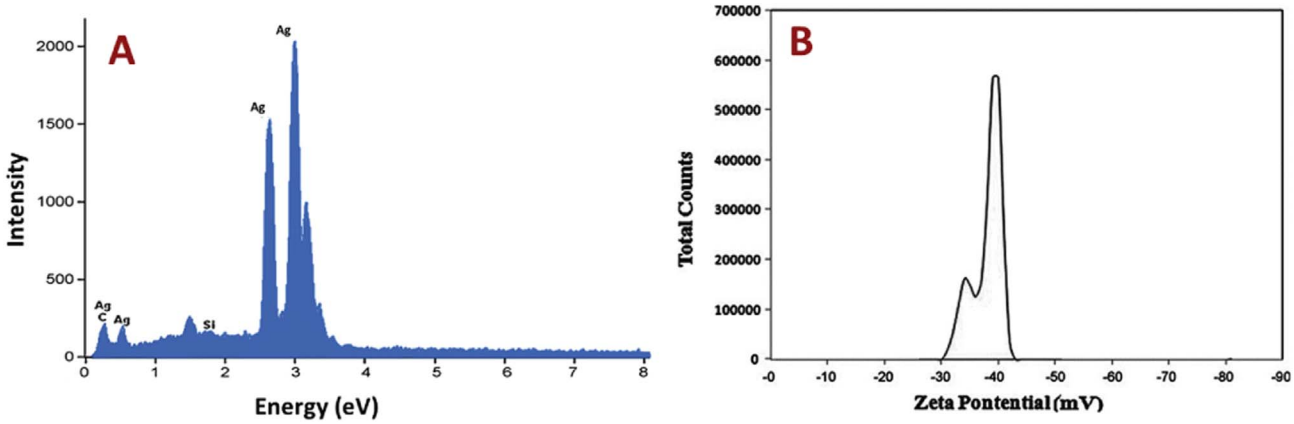

Fig. 4. EDS spectrum (A) and zeta potential (B) of AgNPs synthesized by using basalin.