

## INTRODUCTION

The word 'Ayur' means life, while 'Veda' means science. Therefore, Ayurveda literally means the 'Science of Life'. It is not just a medicinal system, but also a way of life. Ayurveda deals with the physical, as well as spiritual health. With larger commercial interest, the western countries promoted modern medicine, inspite of its high cost and side effects. However, realising the drawbacks of allopathic medicine, the world is turning back to herbal medicines. Presently, about 80% of the world population is still dependent on medicinal plants for health care and 20% of the drugs in pharmaceutical firms are of plant origin, either extracted from the plants or synthetic derivatives of these plant species (Merghoub *et al.*, 2009).

India has a wealth of medicinal plants most of which have been traditionally used in Ayurveda, Unani systems of medicine and by tribal healers for generation. Medicinal plants form the backbone of traditional system of medicine in India. Pharmacological studies have acknowledged the value of medicinal plants as potential source of bioactive compounds (Ahmed *et al.*, 2012). Medicinal plants are gifts of nature to cure limitless number of diseases among human beings. The reason for using them as medicine lies in the fact that they contain chemical components of therapeutic value. The medicinal value of plants lies in some chemical substances (usually secondary metabolites), that produce a definite physiological action on the human body. The most important of these bioactive compounds of plants are alkaloids, flavonoids, tannins and phenolics (Dhanamani *et al.*, 2011).

A free radical can destroy a protein, an enzyme or even a complete cell. Free radicals can multiply through a chain reaction mechanism resulting in the release of thousands of the cellular oxidants (Ahmad and Khan, 2012). Cells can become so badly damaged that DNA codes can be altered and immunity can be compromised. Contact with a free radical or oxidant on the scale can create

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cellular deterioration, resulting in diseases like cancer (Gautam and Shivhare 2011). Reactive oxygen species (ROS) are an entire class of highly reactive molecules derived from the metabolism of oxygen. ROS, including superoxide radicals, hydroxyl radicals, and hydrogen peroxide, are often generated as by products of biological reactions or from exogenous actors. ROS play positive roles in cell physiology; however, they may also cause great damage to cell membranes and DNA, inducing oxidation that causes membrane lipid peroxidation, decreased membrane fluidity, and DNA mutations leading to cancer, degenerative and other diseases (Narendhirakannan and Thomas, 2010).

To protect the cells and organ systems of the body against reactive oxygen species, humans have evolved a highly sophisticated and complex antioxidant protection system. It involves a variety of components, both endogenous and exogenous in origin, that function interactively and synergistically to neutralize free radicals (Liu *et al.*, 2012). Antioxidants have been reported to prevent oxidative damage caused by free radical, it can interfere with the oxidation process by reacting with free radicals, chelating, catalytic metals and also by acting as oxygen scavengers (Pervaiz and Clement 2007). Plant species have been investigated in the search for novel antioxidants. It has been mentioned the antioxidant activity of plants might be due to their secondary metabolites. Alkaloids, flavonoids and phenolics are a group of compounds with known properties which include free radical scavenging, inhibition of hydrolytic and oxidative enzymes and anti-inflammatory action. Some evidence suggests that the biological actions of these compounds are related to their antioxidant activity (Chakraborty and Ghorpade 2010).

Cancer is medically known as neoplasm which means a relatively autonomous growth of tissues and commonly defined as an uncontrolled growth of cells, with loss of differentiation and commonly with metastasis, spread of the cancer to other tissues and organs. A metastasis is a secondary growth originating from the primary tumour and growing elsewhere in the body. In developed nations at least one in five of the populations can expect to die of cancer. After

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cardiovascular diseases, it is the second cause of death amongst the global population. Cancer is the cause of more than six million deaths each year in the world (Patel *et al.*, 2010).

The “war on cancer” is now in its fourth decade since the National Cancer Act was passed in 1971. Cancer cells usually invade and destroy normal cells. These cells are born due to imbalance between the free radicals and antioxidants in the body and by correcting this imbalance, the cancer may be treated (Balasubramanian and Rangunathan, 2012).

Over the last two decades, multiple natural phytochemicals with diverse chemical structures such as alkaloids, flavonoids, tannins (Jayshree and Thaware 2012), curcumins (Yogesh and Nayak, 2012) and polyphenols have been proposed as chemopreventive agents (Rahman *et al.*, 2011). Different antioxidative enzymes including catalase, superoxide dismutase, glutathione S-transferase, glutathione peroxidase and glutathione reductase as well as antioxidative molecules such as Vitamin A, E, C and reduced glutathione are able to arrest those reactive oxygen species and reactive nitrogen species when prolonged exposure to xenobiotics and infections (Kaur and Kumar, 2009).

Nanotechnology can be termed as the synthesis, characterization, exploration and application of nanosized (1-100nm) materials for the development of science. It deals with the materials whose structures exhibit significantly novel and improved physical, chemical, and biological properties, phenomena, and functionality due to their nano scaled size. Because of their size, NPs have a larger surface area than macro-sized materials. The intrinsic properties of metalNPs are mainly determined by size, shape, composition, crystallinity and morphology. Thus offering many new developments in the fields of biosensors, biomedicine, and bionanotechnology. Nanotechnology is also being utilized in medicine for diagnosis, therapeutic drug delivery and the development of treatments for many diseases and disorders. Nanotechnology is an enormously powerful technology, which holds a huge promise for the design and development

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of many types of novel products with its potential medical applications on early disease detection, treatment, and prevention (Ponarulselvam *et al.*, 2012).

The NPs are regarded to be the ideal vehicles for antitumor drug delivery because their hydrophobic inner core is an appropriate reservoir for hydrophobic anticancer drugs and their hydrophilic outer shell facilitates the avoidance of the reticuloendothelial system, long blood circulation, and the improvement of enhanced permeation and retention effect in tumor tissue (Zhang *et al.*, 2011). NPs are about one hundred to ten thousand times smaller than human cells, can offer unprecedented interactions with biomolecules both on the surface and inside the cells, which may revolutionize cancer diagnosis and treatment (Wang *et al.*, 2011).

Researchers have focused towards coupling these anticancer agents with nanobased encapsulation technology for the development of targeted delivery of chemotherapeutics directly to cancer cells, followed by their slow release in potentially sustainable levels that may provide superior efficacy and lower toxicity for treating primary or advanced metastatic tumors (Renugadevi *et al.*, 2012).

Green synthesis provides advancement over chemical and physical methods as it is cost effective, environment friendly and easily scaled up for large scale synthesis with a single-step method (Prabhu *et al.*, 2010). Green NPs synthesis has been achieved using environmentally acceptable plant extract which act as reducing and capping agents (Devi *et al.*, 2012). The most prominent nanoproduct is nanosilver. Nanosilver particles are generally smaller than 100 nm and contain 20–15,000 silver atoms. AgNPs have been shown to possess intrinsic cytotoxic activity (Ravi and Rao 2012).

The role of AgNPs as an anti-cancer agent should open new doors in the field of medicine. The AgNPs are also reported to be nontoxic to human and most effective against bacteria, viruses, and other eukaryotic micro-organisms at very low concentration and without any side effects. The design of smart multifunctional nanosystems for intracellular imaging and targeted therapeutic applications requires a thorough understanding of the mechanisms of NPs entering and leaving

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the cells. For biological and clinical applications, the ability to control and manipulate the accumulation of NPs for an extended period of time inside a cell can lead to improvements in diagnostic sensitivity and therapeutic efficiency. This when revealed completely would eliminate the use of expensive drugs for cancer treatment. In general, AgNPs should serve as one of the best ways of treating diseases that involve cell proliferation and cell death (Mohammadzadeh, 2012).

*Gloriosa superba* is commonly known as glory lily and it is a perennial creeper in the family Liliaceae, growing naturally in many countries of tropical Asia including Bangladesh, India, Sri Lanka, Malaysia and Myanmar (Banu and Nagarajan, 2012). This plant is used as an ayurvedic medicinal herb to cure diseases like arthritis, gout, ulcers, and bleeding (Jain and Suryavanshi, 2010). In the Indian systems of medicine, the tubers are used as tonic, antiperiodic, antihelmenthic and also against snake bites. There is no systematic scientific studies on the antitumorigenic role of methanolic extract of *Gloriosa superba* and its silver NPs in Swiss albino mice. This fostered our attempts to evaluate the plant extract against cancer, as they are less likely to cause serious side effects. Hence, the present research entitled **“Antioxidant and Antitumorigenic efficacy of methanolic extracts of *Gloriosa superba* and Silver Nanoparticles of methanolic extracts of *Gloriosa superba* to DLA tumor cells”** is organized with the following objectives and hypothesis:

1. To characterize MGsSTL and AgMGsSTL by phytochemical screening, HPTLC, UV-Visible Spectroscopy, FT-IR, SEM with EDX, TEM, DLS, Zeta-Potential and XRD analysis.
2. To evaluate the *in vitro* antioxidative and antitumorigenic efficacy of the methanolic extract of *Gloriosa superba* seed, tuber and leaves (MGsSTL) and AgNPs of methanolic extract of *Gloriosa superba* seed, tuber and leaves (AgMGsSTL).
3. To evaluate the *in vivo* antioxidative and antitumorigenic potential of the MGsSTL and AgMGsSTL in Dalton lymphoma ascites tumour induced Swiss albino mice.
4. Null hypothesis was proposed that there is a no significant difference in the antioxidant and antitumorigenic effect between the extracts of MGsSTL and AgMGsSTL both in *in vitro* and *in vivo* studies.