INTRODUCTION

Medicinal plants are invaluable for the survival of both human and animal population globally. They are a rich source of phytochemicals, which can be used to treat various ailments of mankind (Rajamurugan et al., 2013; Aderiye and David, 2014). In India, natural products derived from medicinal plants have been used traditionally for the treatment of various disorders including cancer (Mamidala and Gujjeti, 2013).

But the use of these medicinal plants needs proper validation and documentation in order for utilizing it as a drug for treating various pathophysiological conditions (Maroyi, 2013; Anita and Retna, 2013; Manjula and Mamidala, 2013). About 6000 medicinal plants have been estimated to be present in India, of which, only 3000 plants have been proved to have medicinal value and still many remains unexplored (Jagatheeswari et al., 2013).

Cancer is one of the most dreadful diseases that is globally distributed among the world’s population. Cancer occurs due to excessive free radical damage, which ultimately causes damage to the genetic material DNA, protein and lipids. This DNA damage leads to mutations that cause normal cells to transform into a cancer cell (Roszkowski, 2014). Excessive production of free radicals occurs due to increased production of reactive oxygen species (ROS) and reactive nitrogen species (RNS). This leads to a condition of increased oxygen environment called oxidative stress. In cancer cells, increased levels of reactive oxygen species have been found, which causes uninterrupted cell proliferation and leads to tumour development (Gorrini et al., 2013; http://cancerfightingstrategies.com/antioxidants-for-cancer.html).

Failure of apoptosis and increased rate of cell survival occurs due to DNA damage that results in cancer development. Apoptosis is the major form of programmed cell death, which takes place in all the cells to maintain homeostasis and cellular integrity. Cancer treatment therapies target this apoptotic pathway by
increasing apoptosis in cells and thus preventing cancer (Kalimuthu and Se-Kwon, 2013; Zhao et al., 2014).

The tumour development is induced by the presence of increased levels of reactive oxygen species (Maiti, 2012). Antioxidants and phytochemicals present in the medicinal plants have been found to arrest the growth of cancer cells by promoting apoptosis, thus preventing the progression of cancer (Alok et al., 2014). The free radical scavenging activity of the medicinal plants or compounds is the major mechanism that is responsible for the anticancer property of the plant (Lee et al., 2014a). The intake of foods rich in antioxidant compounds helps to prevent cancer development (Raffoul et al., 2012).

In vitro models are used in biological research in order to minimise the sufferings to animal models. The in vitro models mimic the biological system existing inside the human body and provide researchers a useful tool for analyzing various parameters under controlled conditions. The results are more accurate and reproducible and are free from the influence of complex biological parameters (Yamuna and Padma, 2013; Sumathi et al., 2013a).

Breast cancer is the most common type of cancer among women in both developed as well as developing countries (Pandey and Chandravati, 2013). The incidence of breast cancer cases has been increasing among the Indian women and it has been estimated that by the end of 2030, there will be about 2,00,000 new breast cancer cases (Datta et al., 2012; Sharma et al., 2013a). In India, about 1 in 28 women develop breast cancer during their life time. This incidence is 1 in 22 in rural areas and in urban areas, 1 in 60 women are prone to the development of breast cancer (https://tmc.gov.in/cancerinfo/breast/breast.html).

Women with breast cancer live almost 10 years more in developed countries after diagnosis and treatment than the women in developing countries due to lack of awareness and poor diagnosis. Most of the women in developing countries were diagnosed with breast cancer only at the later stages of development which makes the treatment methods ineffective because the cancer cells at advanced stages exhibit therapy resistance (http://www.ns.umich.edu/new/releases/21167-early-breast-cancer-diagnosis-survival-rates-low-in-rural-india).
There are three most common types of breast cancers, which are classified based on the receptors expressed in these cells. They are Estrogen / Progesterone positive (ER\(^+\)/PR\(^+\)), Her 2 positive (Her\(^2+\)) and triple negative breast cancer (ER\(^-\),PR\(^-\),Her\(^2-\)) (http://www.breastcancer.org/symptoms/diagnosis). In the current scenario, different types of cancer therapies are employed for breast cancer treatment. They are chemotherapy, radiation therapy, hormonal therapy and targeted therapy (http://www.webmd.com/breast-cancer/guide/treatment).

All these therapies cause severe side effects to the normal cells. The targeted therapy, is not only specific to the cancer cells alone, but it is also specific to particular type of cancer and is also very expensive (Abdollahi and Shetab-Boushehri, 2012). Various plant extracts in different combinations find their use in a number of pharmaceutical preparations used in Siddha and Ayurveda. The natural products derived from the medicinal plants provide an excellent source of cancer medication. The use of natural products in cancer therapy offers many advantages because they not only kill the cancer cells, but also some natural agents have been found to render protection to normal cells (Chanda and Nagani, 2013).

Several anticancer compounds isolated from the medicinal plants have been clinically approved and used in pharmaceutical preparations currently used for the treatment of cancer. These include vinblastine, vincristine (from Catharanthus roseus), navelbine (Vinca minor), etoposide, teniposide (from Podophyllum peltatum), taxol (from Taxus brevifolia), taxotere (from Periwinkle), topotecan and irinotecan (Camptothecan derivatives). Various other natural plant-derived components such as plumbagin, quercetin, berberin, artemisinin, lupeol, betulinic acid and curcumin have been identified as potential source of anticancer drugs (Patil et al., 2013). So, the exploration of active components from plant sources is an active area of research that makes it possible for the development of new pharmaceutical preparations.

Although various natural and synthetic compounds have been used for the treatment of cancer, the molecular mechanism of action of these agents on cancer cells is still not clearly understood. The chemotherapeutic drugs used for cancer treatment are capable of retarding growth of both normal as well as cancer cells. Hence, there is a need for new drug which can induce cell death only in cancer cells
but cause potentially less or no toxicity to normal cells. Thus, studies to find the underlying mechanism of action of these agents on cancer cells are required which will help in the development of targeted therapies (Raffoul et al., 2012).

Curcuma amada Roxb is a well known rhizomatous herb which is commonly known as Mango ginger that belongs to the family Zingiberaceae (Ginger family) that is widely cultivated in various parts of South India. C. amada rhizomes have been used for culinary purposes and pickle preparations in South India. This plant has been proved to have many biological activities such as antioxidant (George et al., 2013), anti-inflammatory, antihelminthic (Randeep et al., 2011), hypoglycemic, anti-hyperglycemic (Syiem et al., 2010), cytotoxic, platelet aggregation inhibitory and antimicrobial activities (Policegoudra et al., 2011).

Traditionally, it has been used as an appetizer, alexiteric, antipyretic, aphrodisiac, diuretic, emollient, expectorant, laxative and to cure biliousness, itching, skin diseases, bronchitis, asthma, cough and inflammation (Policegoudra et al., 2011). The rhizomes of this plant have been included in various ayurvedic preparations and traditionally it has been used to treat digestive disorders. However scientific validation on this plant is very scarce.

With this background, the present study is focussed on exploring the anticancer and apoptosis inducing activity of the leaves and the rhizomes of the medicinal plant C. amada Roxb.

1.1 Hypothesis

The hypotheses set up for the present study are as follows:

Null hypothesis ($H_0$): The methanolic extract of the leaves and the rhizomes of C. amada do not possess antioxidant and anticancer properties.

Alternate hypothesis ($H_A$): The methanolic extract of the leaves and the rhizomes of C. amada possess strong antioxidant and anticancer activities.

Hence, the present study was formulated with the following objectives to test the above mentioned null and alternate hypotheses.
• To assess the free radical scavenging activity of various extracts of the leaves and the rhizomes of *C. amada* Roxb and the antioxidant modulating activity of the extracts using oxidatively stressed precision-cut goat liver slices

• To evaluate the cytotoxic activity induced by the extracts in eukaryotic model organism yeast

• To evaluate the anticancer potential of the extracts using breast cancer cell lines

• To determine the phytochemical constituents present in the leaves and the rhizomes of *C. amada*.

A brief review of the vast literature available, relevant to the present study, is presented in the next chapter.