Cancers is the second most leading disease next to cardiovascular diseases. The WHO, the prevalence of cancer is expected to reach as high as 15 million new cases by 2020. In developed countries, oral cancer is a common neoplasm which accounts in 5% of all other human cancers. Epidemiologic studies have showed that environment and personal habits, particularly in use of tobacco and alcohol consumption, seems to be major etiologic factors for the development oral cancer. Several molecular mechanisms implicated in the malignant transformation and progression of oral cancer is still not clear. However, some predictive biomarkers are likely to be useful in identifying patients who would benefit from more intensive treatment.

The HBP carcinogenesis is an excellent animal model for the induction of oral squamous cell carcinoma by chemical carcinogens of DMBA and if is useful for investigating as chemopreventive agents. DMBA induced HBP carcinogenesis is biochemically and histologically similar to human oral cancer. Under normal physiological conditions, free radicals are generated in subcellular compartments were scavenged by antioxidant systems. DMBA carcinogen, disrupt the pro-oxidant–antioxidant balance which leads to antioxidants depletion to the normal cells (Li et al., 2002). Krishnaveni and Mirunalini, (2012) were reported that levels of LPO and antioxidants are decreased in tumor tissues due to prolonged tumor cells proliferation. ROS is major biological process which plays an important role in carcinogenesis. Several evidence have established that excessive ROS generation cause oxidative damage such as DNA, lipids, and proteins and enzymatic and non enzymatic antioxidants (Ott et al., 2007).
There is increasing evidence that human cancers can be prevented by favouring the intake of protective factors that modulate the defense mechanisms of the host organism. Liver, is major detoxification organ, it metabolizes several toxic substances like mutagens and carcinogens. The phase I enzymes (CYP-450, CYP-5) convert hydrophobic compounds to reactive electrophiles by oxidation, hydroxylation and reduction reactions. Phase II enzymes (GST, GR, GSH) primarily catalyze conjugation reactions. Many chemopreventive agents are involved in the induction of Phase II detoxifying enzymes leads to protection of cells/tissues against exogenous and/or endogenous carcinogenic intermediates.

Glycoproteins are the major constituents of cell membrane and play an important role in cell differentiation, cell proliferation and cell-cell interaction. Hence, the measurement of serum glycoconjugates in oral precancerous and cancerous lesions are useful in the diagnosis of cancer patients and in experimental animals. Aberrant glycosylation in cell membrane are the important events in neoplastic cell transformation. Elevated serum levels of sialic acid, fucose and certain glycoprotein in various carcinomas, including oral cavity cancer have been reported that elevated glycoconjugates are released into the circulation through increased turn over, secretion and/or shedding from malignant cells including oral cancer.

Oncogenesis is a multistep process such as initiation, promotion and progression occur normal cells are transformed into cancer cells. It is characterized by a progression of changes on genetic and molecular level that ultimately reprogram a cell to undergo uncontrolled cell division, and thus forming a malignant tumor development. Cell proliferation, differentiation, survival and apoptosis are tightly regulated by a number of signaling transcription factors activate molecules like cytokines, growth factors, and hormones in multicellular organisms. These extracellular regulators molecules
usually serve as ligands for cellular receptors and to communicate with the nucleus in the cell through a network of intracellular signaling pathways (Khan and Bisen, 2013; Chow, 2010). In cancer cells, dysregulated cell signaling events and proliferation may occur through over expression or mutation in the genes that normally play a role in the regulation of cell proliferation and survival, dysfunction of apoptotic genes leading to uncontrolled cell growth to develop malignant tumor (Chow, 2010).

Ginger (*Zingiber officinale Roscoe*) has been widely used as a condiment throughout the world for centuries. In Asian countries particularly China and India, ginger has been used as herbal medicine to treat a various disease such as inflammation, dyspepsia, nausea, vomiting, pain, the common cold and diarrhoea (Ali et al., 2008). Several biologically active components present in ginger are reported to be phenylpropanoid-derived compounds such as gingerols, shogaols, paradoxol and gingerone. As dehydrated products of gingerols, shogaols exist in fresh ginger at low levels, the larger amounts present in dried ginger (Jolad et al., 2005).

Earlier studies have indicated that [6]-shogaol has potent anti-inflammatory and anticancer effects. For instance, the phenolic agent of [6]-shogaol has been shown to induce apoptosis via the production of ROS and activation of caspase in human colorectal carcinoma cells (Pan et al., 2008b). In another study, [6]-shogaol reduce gastric cancer viability by impairing tubulin polymerization (Ishiguro et al., 2007). In addition, [6]-shogaol has been shown to be effective at inhibiting the expression of inflammatory mediator enzymes iNOS and COX-2 (Pan et al., 2008a) and also suppressed the TRIF-dependent signalling pathway of Toll-like receptors by targeting TBK1 (Park et al., 2009). Hence, no scientific reports were available in the literature about its chemopreventive and anti-cancer effects of [6]-shogaol against DMBA induced HBP carcinogenesis.
2.1. The specific objectives of the present study

_In-vitro study_

- To investigate the free radical and antioxidants potential of [6]-shogaol using various free radical scavenging assays.
- Screening cytotoxicity potential of [6]-shogaol against Hep-2 cells
- To evaluate the apoptotic inducing properties of [6]-shogaol by analysing apoptotic morphological changes, and modulate apoptotic markers such as Bax, Bcl-2, Caspase-3, Caspase-9, Cytochrome c in Hep-2 cells.

_In-vivo study_

- To evaluate the dose response and chemopreventive effect of [6]-shogaol on lipid peroxidation, antioxidants status and histopathological changes during the DMBA induced oral carcinogenesis.
- To investigate the detoxifying potential of [6]-shogaol against DMBA induced toxic metabolites by measuring the status of phase I and II detoxifying enzyme.
- To examine the protective effects of [6]-shogaol on cell membrane integrity by measuring the levels of cell surface glycoconjugates in DMBA induced HBP carcinogenesis.
- To evaluate the effect of [6]-shogaol on inflammation and cell proliferative markers inhibition through NF-κB/AP-1 signaling in 7,12-dimethylbenz(a)anthracene (DMBA) induced hamster buccal pouch carcinogenesis.
- Explore the apoptotic, angiogenesis and anti-invasive role of [6]-shogaol targeting through JAK-1/STAT-3 and PI3K/AKT signaling in DMBA induced oral carcinogenesis.