



Research Paper

Cancer Research Anti-Cancer Activity PHPC Compound

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Research Objective

The Study indicates that research provides chemo preventive effects

Significant reduction in cancerous cells

Indicative suppression of growth of tumor

Quantifying and analyzing DNA damage in individual cells

Abstract

PHPC Compound is the patent and proprietary medicine developed by Benmoon Pharma Research Pvt Ltd., Ahmedabad. The entire study was planned to do evaluation of efficacy and safety of PHPC Compound in experimental animal's models. First it was screened in-vitro using breast cancer cell line using MTT assay method, wherein it has shown significant reduction in viable cancerous cells.

After promising result in in-vitro study, safety was checked using Acute toxicity study (OECD 425), wherein it was found safe till the dose of 2000-5000mg/kg, orally.

Further, for long term usage of this formulation, its sub-chronic (90 days) oral toxicity study was done (AYUSH & OECD 408 guideline) in rats and guinea pigs, wherein it shows no significant toxic sign, symptoms and in histology too. To check whether it retards toxic effects against chemotherapeutic agents induced toxicity, it was evaluated against 5-FU model, wherein also it has shown chemo-preventive activity.

To check its effectiveness against breast cancer, it was further screened against DMBA-induced cancer model, wherein also it has shown significant reduction in occurrence of tumor, reduction in tumor size and volume. DMBA induced breast cancer by DNA mutation and increasing free radicals level. The treatment of PHPC Compound reduces free radical levels as evident by significant increase in SOD and Catalase level. Further, it reduces serum level of SGOT and SGPT level, which usually get secreted during tissue damage.

Further to check the effectiveness of the PHPC Compound on DNA damage in individual cells of cancer cell line. In the present study, in 5-FU (5.0µg/ml) treated cell line, there was reduction in % Head and increase in % Tail, which indicates DNA damage in L929 and MCF-7 cell line. Wherein in case of Test drug (20, 40 and 60 µg/ml) groups, there was significant increase in % Head and decrease in % Tail, which indicates that test drug provides chemo preventive effects. In brief, PHPC Compound has shown promising level of safety and efficacy in experimental animal models.

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I. Introduction

The purpose of the research study on cancer is to develop safe and effective methods to prevent, detect, diagnose, treat, and, ultimately, cure the collections of diseases we call cancer. Ideas for new cancer research studies are often inspired by findings from earlier research, research on other cancers, and even findings from research done on other diseases, such as diabetes or immune disorders. Its aim is to reduce the number of deaths from cancer.

The research reports that covers cytotoxicity study evaluated for cytotoxicity against human adenocarcinoma cell for performing Anti - Cancer Activity effect on cellular DNA damage with his research called PHPC Compound has shown significant reduction in occurrence of tumor, reduction in tumor size and volume, having conducting clinical researches, investigating methods of prevention, diagnosis & treatment studies for several years. The results revealed that the formulation showed significant cytotoxicity on cell line. Overall, the cell growth inhibition by the PHPC observed in this study synergistic response rates. In brief, PHPC Compound has showing promising level of results in experimental models. To check the effect of PHPC Compound on cellular damage against normal cell line and breast cancer cell line using comet assay method.

Cell count, Splitting of cells, ratio analysis of the cells and cells viability following the procedure mentioned allow the cell to grow and divided into groups.

To check the effect of formulation PHPC Compound on cellular DNA damage against normal celline and against breast cancer cell line MCF 7 using single cell gel electrophoresis technique comet assay. The scope covers comet assay of given test samples as per in house method. Evaluation of DNA damage for visualization of DNA damage, observations are made of SyBR-stained DNA using a 40x objective on a fluorescent microscope.

Women breast cancer is the most important cause of mortality in the world. Now a day, some cytotoxic agents are used for its treatment including 5- flurouracil, doxorubicin, daunorubicin, bleomycin, and cisplatin. However, they are costly and known to induce several side effects such as myelosuppression, anemia, and most importantly the generation of cellular resistance. For this, it is important to find alternative therapies or drugs to overcome these drawbacks. Therefore in the present study, the polyherbal formulation screened for its anticancer activity using MCF-7 cell lines. The formulation PHPC Compound was subjected to cell proliferation assay by MTT. The results revealed that the formulation showed significant cytotoxicity on MCF-7 cell line. Overall, the cell growth inhibition by the polyherbal formulation observed in this study synergistic response rates.

II. Summary of Findings

Mammary tumors were successfully induced by oral administration. PHPC Compound produced significant anti-cancer activity, which was evident by significant reduction in incidence of solid tumor in PHPC Compound treated group. This was clearly indicated by means of results of tumor as compared to diseases control group and histopathology of mammary gland. PHPC Compound significantly increased the level of antioxidant enzymes like SOD and catalase, which were reduced in case of diseased controlled groups. This indicates chemo-protective effect of PHPC Compound.

OBJECTIVE

To study the anti cancer activity of Polyherbal formulation PHPC Compound.

SCOPE

The scope covers cytotoxicity study by using MTT assay on MCF-7 human breast cancer.

III. Methodology

List of Pharmacological Activities Done for PHPC Compound Sr. No.	Type of Study	Experimental Model Used
1.	In-vitro anti-cancer study	MTT assay using breast cancer line
2.	Acute Toxicity Study	Acute Oral Toxicity study as per OECD 425 guideline
3.	Chemo- preventive Study	Protective effect of PHPC Compound against 5-FU induced toxicity study
4.	Sub chronic toxicity study	90 days oral toxicity study as per AYUSH and OECD 408 guideline.
5.	In- vivo Anti-cancer activity	DMBA induced breast cancer Model.
6.	Comet assay	Effect on cellular DNA damage

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MTT ASSAY

The formulation PHPC Compound was evaluated for their cytotoxicity against human adenocarcinoma cell line of breast (MCF-7) cancer using MTT assay. Amongst different concentration of the formulation, 100 µl/ml test sample shows 92.6% cytotoxicity and remaining concentration that is 200, 400, 600, 800 and 1000 µl/ml test sample shows 100% cytotoxicity towards MCF-7 cell line. Further, standard sample (5-fluorouracil) at different 100, 200, 400, 600, 800 and 1000µl/ml standard sample showed 83.32 %, 97.59 % , 100 %, 100 %, 100% and 100 % cytotoxicity respectively. The formulation and 5- fluorouracil showed significant cytotoxicity ($p < 0.001$) MCF-7 cancer cell lines as compared to control (Figure 3, Annexure-I). To support the MTT assay cytotoxicity was also studied by counting the viable cells in hemocytometer using microscope.

From 48 hours of study where the cells were allowed to grow for 48 hrs in presence of test sample it was found that 100µl/ml test sample show least cytotoxicity while with increase in concentration of test sample cytotoxicity increased such as 200 and 400µl shows 29% cytotoxicity, 600 and 800 µl/ml shows 72% and 1000µl/ml sample shows 100% cytotoxicity.

Research Methodology

A Report Of Anti-cancer activity (In vitro) of herbal formulation-PHPC Compound

A Report Of Acute Oral Toxicity Study Of PHPC Compound

To evaluate protective effect of in 5-fluorouracil (5 FU) induced toxicity

A Report Of Sub-chronic (90-days) Oral Toxicity Study of PHPC Compound

A Report of Study of PHPC Compound in 7,12-Dimethylbenz(a)anthracene induced Breast cancer

Evaluation of effect of formulation "PHPC Compound" on cellular DNA damage

Protective effect of PHPC Compound against 5-FU induced toxicity study

IV. Recommendation

Women breast cancer is the most important cause of mortality in the world. Now a day, some cytotoxic agents are used for its treatment including 5- fluorouracil, doxorubicin, daunorubicin, bleomycin, and cisplatin. However, they are costly and known to induce several side effects such as myelosuppression, anemia, and most importantly the generation of cellular resistance. For this, it is important to find alternative therapies or drugs to overcome these drawbacks. Therefore in the present study, the polyherbal formulation screened for its anticancer activity using MCF-7 cell lines. The formulation PHPC Compound was subjected to cell proliferation assay by MTT. The results revealed that the formulation showed significant cytotoxicity on MCF-7 cell line. Overall, the cell growth inhibition by the polyherbal formulation observed in this study synergistic response rates. It has known that cytotoxicity is mainly through apoptosis or necrosis.

V. Conclusion

PHPC Compound significantly decreases the level of WBC count, which was increased in case of diseased control group and indicative of host immune response due to tumor growth. But this reduction in WBC count by PHPC Compound treatment indicates that it decreases host immune response, which may be indicative of its suppression of growth of tumor

Keywords:- cancer, cancer diagnosis, cancer treatment, cancer research, cancer cell, oncology, tumor, breast cancer, chemotherapy, radiation therapy, tumor size, DNA, tumor growth, research and development, cancer phase, metastatic, malignant cells

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- [2]. Rina H Gokani Pharmacology and Toxicological Department 24/02/2016 This study performed according to the protocol, under the Inspiration of GLP testing facility, standard operating procedures and under CPCSEA regulation. This study was approved by committee of IAEC with reference no. ARL/PT/037/2015.
- [3]. Ms. Shruti C. Shukla Biotechnology Department Research Associate 22/02/2016 After single administration of test dose in animals, different parameters were observed as specified under OECD Guideline 423. Acute Oral Toxicity Study of PHPC Compound . The scope of the study is to Evaluate the effect of PHPC Compound in 5-fluorouracil induced toxicity Dr. Girish Vyas IAEC Committee 20/04/2015 Standard laboratory safety procedure was employed for handling the dose formulations. Specifically, gloves and eye protection were worn while administering doses. The manufacturer of the test articles was supplied a Material Safety Data Sheet (MSDS) and/or other pertinent documentation regarding safety. Mr. Darshit Joshi Pharmacology committee of IAEC with reference no. ARL/PT/033/2015 As shown in Open Field test and Actophotometer test, there were decreased in Locomotors activity up to four hours after dose administration as observed in **Annexure 1**.

- [4]. Mr Jaswant Parmar M Pharma Pharmacology committee of IAEC with reference no. ARL/PT/033/2015 High quality food diet from Pranav agro science, Pune were provided and deionised water provided with *ad libitum*, except during protocol-specified periods of fasting. No contaminants were known to be present in the certified diet that would interfere with the results of the study. Results of the food and water analysis were reviewed periodically by a staff veterinarian or Scientist Accuprec Research BSCIC GLP detailed clinical observation ARL/164/2015 As per OECD guideline 423, The LD₅₀ of PHPC Compound found to be **2000-5000mg/kg, orally**