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Phytochemical and Anticancer Studies of *Cinnamomum malabatrum*

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ABSTRACT

Background: *Cinnamomum malabatrum* is also called as wild cinnamon, country cinnamon and as malabathrum, it belongs to the family Lauraceae, that is endemic to western ghats of India. Various chemical classes of drugs from plants like flavonoids and other phenolics, terpenes and terpenoids, some organic acids like Benzoic acids, cinnamic acid and their derivatives, alkaloids, tannins that have many therapeutic properties. It has also been found that these compounds lead to cytotoxic effects. **Aim & Objective:** The present study is undertaken to evaluate the phytochemical and anticancer activity of *Cinnamomum malabatrum* (stem bark). **Methods:** The stem bark of the plant was extracted by the Soxhlet apparatus with different solvent like petroleum ether, chloroform, acetone, ethanol and Water. Preliminary phytochemicals were performed with different chemical methods. The anticancer activity of ethanolic and aqueous extract were determined. **Conclusion:** The extraction of aqueous and ethanol was in a concentration-dependent manner and significantly with controlling cells inhibited the growth of cancer cells. This inhibition was made through induction of apoptosis and due to the presence of effective compounds which could be considered as valuable natural sources for the isolation of anti-cancer compounds.

INTRODUCTION

For centuries, plants have been used both in the treatment and prevention of diseases, as they contain a large amount of compounds with a broad spectrum of biological activity. The constant interest in acquiring new plant-based compounds that can support the treatment of many diseases leads to the dynamic development in the field of research of compounds obtained from plant material [1, 2]. Plant extracts are used as anti-inflammatory and antimicrobial agents, and numerous studies have been carried out in terms of the development and identification of new anti-cancer agents, which have been repeatedly confirmed in studies [3]. Currently, there is a lot of research carried out around the world in order to identify new plant species with anti-cancer activity that are an alternative to toxic chemotherapeutic agents [4, 5]. Due to the progressive resistance of cancer cells to applied chemotherapy, the identification of new plant compounds represents a huge potential for research. It is important that most plant ingredients are safe to use [6, 7].

Cinnamomum genus, the *C. malabatrum* (Burm.f.) J.Presl is an endemic medicinal plant that belongs to the Western Ghats, Kerala, India. Limited studies are available on the essential oil of the plant; Leela et al. [8] indicated the chemical composition of the essential oil of *C. malabatrum* where (E)-Caryophyllene (28.6%), (E)-Cinnamyl acetate (15.1%) and Bicyclogermacrene (14.4%) were the predominant compounds. Later, a study by Sriramavaratharajan and Murugan [9] reported the predominant compounds as β-Phellandrene (12.0%) and linalool (15.4%). The present study, therefore, aimed to extract the essential oil from the *C. malabatrum* leaves and analyze its chemical composition. Further, the radical quenching properties of the essential oil and its enzyme-inhibitory properties were evaluated using in vitro models. The enzyme-inhibition activity was assessed in terms of diabetes-associated enzymes; the α-amylase and α-glucosidase are major enzymes associated with carbohydrate metabolism and thereby contribute to type 2 diabetes mellitus [10, 11], and are a prominent target for antidiabetic drugs [12, 13]. The activation of polyol pathway enzymes aldose reductase and sorbitol dehydrogenase plays a crucial role in the microvascular complications of diabetes [14, 15, 16]. The antibacterial activity was also determined using two methods: the disc diffusion method and minimum inhibitory concentrations. However, this species has not yet been described either in terms of its chemical composition or its potential for biological activity. Therefore, the aim of the study was the phytochemical analysis of different extracts obtained from the stem bark of the *C. malabatrum*, as well as evaluation of their anticancer activity.

MATERIALS AND METHODS

Preparation of Extract: The selected plant part was air dried under shade. The powder was passed through sieve No 40 and stored in an airtight container for further use. The collected, cleaned powder material of *Cinnamomum malabatrum* were used for the extraction purpose. 800 g powder of *Cinnamomum malabatrum* was evenly packed in the separate Soxhlet apparatus. It was then defatted by keeping in petroleum ether for 24 hours. The solvents used were purified before use. The extraction method used was Continuous Hot Percolation and carried out with various solvents, for 72 hours. [17, 18]

Petroleum Ether Extract: The shade dried coarsely powder of plants were extracted with petroleum ether (60-80°C), up to 24 hrs. After completion of extraction, the solvent was removed by distillation. Dark green color residue was obtained. The residue was then stored in a desiccators.

Chloroform Extract: The marc left after Petroleum Ether extraction was dried and then extracted with Chloroform (55-56 °C), upt o 72 hrs. After completion of extraction, the solvent was removed by distillation. Dark greenish yellow color residue was obtained. The residue was then stored in a desiccators.

Acetone Extract: The marc left after Chloroform extraction was dried and then extracted with Acetone (55- 56 °C), up to 72 hrs. After completion of extraction, the solvent was removed by distillation. Dark brownish color residue was obtained. The residue was then stored in a desiccators.

Ethanol Extract: The marc left after Acetone extraction was dried and then extracted with ethanol 95% v/v (75-78 °C), upto72 hrs. After completion of extraction, the solvent was removed by distillation. Dark brown color residue was obtained. The residue was then stored in a desiccator.

Aqueous Extract: The marc left after Ethanol extraction was dried and then macerated with distilled water in a 2.5 liters round bottom flask, up to 72 Hrs. 10 ml of chloroform was added daily to prevent fungal growth. After completion of extraction, it was filtered and the solvent was removed by evaporation to dryness on water bath. Brown color residue was obtained. The residue was then stored in a desiccator.

Preliminary phytochemical studies: The pharmacological and therapeutic action of crude drug is determined by the nature of its constituents. Thus, the plant species may be considered as a biosynthetic laboratory not only for the chemical compounds e.g. carbohydrates, proteins and fats that are utilized as a food by humans and animals, but also for a magnitude of compounds including alkaloids, flavonoids, glycosides etc. which exert definite physiological effects. These chemical compounds are responsible for the desired therapeutic properties. To obtained these pharmacological effects, the plant materials are used as such in their crude form or may be extracted with suitable solvents to take out the deride components and the resulting principle being employed as therapeutic agents. A small portion of dry extracts were used for the phytochemical tests for compounds which include tannins, flavonoids, alkaloids, saponins, terpenoids, steroids and cardiac glycosides. [19-21]

Acute toxicity Studies

Determination of LD_{50}: In the acute oral toxicity study, 45 Swiss albino mice were employed to observe the toxicity effects of ethanol and aqueous extract of *Cinnamomum malabatrum*. From the result, mortalities were reported as well as adverse toxicity signs were observed on the tested mice right from the lower dose. The physical appearance such as, fur, raised tails, salivation, paw licking was observed which indicated that the crude extract did affect the animals. [22] The animal models involved in this study were the Swiss albino mice acquired from the Venkateswara Enterprises, Bangalore, India. The experimental procedures relating to the animals were authorized by the Institutional Ethical Committee of Animals before starting the study and were conducted under the internationally accepted principles for laboratory animal use and care (Pharmacology Project no.02/2010) [23].

The parameters evaluated during this assay included body weight of the mice, survival time, paw licking, salivation, stretching/writhing, erect fur, calmness, reduced movement, weakness, coma, convulsion, sleep and death. Three animals were used for each step. The dose level to be used as the starting dose was selected from one of four fixed levels, 5, 50, 300 and 2000 mg/kg body weight. The starting dose level should be that which is most likely to produce mortality in some of the dosed animals.

When available information suggests that mortality is unlikely at the highest starting dose level (2000 mg/kg body weight), then a limit test should be conducted. When there is no information on a substance to be tested, for animal welfare reasons it is recommended to use the starting dose of 300 mg/kg body weight. The time interval between treatment groups is

determined by the onset, duration, and severity of toxic signs. Treatment of animals at the next dose, should be delayed until one is confident of survival of the previously dosed animals. Exceptionally, and only when justified by specific regulatory needs, the use of additional upper dose level of 5000 mg/kg body weight may be considered. For reasons of animal welfare concern, testing of animals in GHS Category 5 ranges (2000-5000mg/kg) is discouraged and should only be considered when there is a strong likelihood that results of such a test have a direct relevance for protecting human or animal health or the environment. [24, 25]

Limit test: A limit test at one dose level of 2000mg/kg body weight may be carried out with six animals (three animals per step). Exceptionally a limit test at one dose level of 5000 mg/kg may be carried out with three animals. If test substance-related mortality is produced, further testing at the next lower level may need to be carried out.

Evaluation of anticancer activity: Swiss albino Mice (20-25 gm) used. The animals were fed with standard pellet diet and water ad libitum. All the animals were acclimatized for a week before use. Dalton‘s ascetic lymphoma cell lines were obtained through the courtesy of Amala Cancer Research Institute, Thrissur, Kerala and were maintained by weekly intraperitoneal inoculation of 1 x 10^6 cells per mice. The alcoholic & aqueous extract of *Cinnamomum malabatrum* was dissolved in normal saline. The alcoholic & aqueous extract of *Cinnamomum malabatrum* stem bark (625 and 500mg/kg body weight) and standard drug 5- fluorouracil (20mg/kg) were used. The animals (Swiss albino mice weighing 20-25 g) were divided into 5 group of 6 animals each. [27-30]

- Group-I (Normal control): Control animals were received normal saline.
- Group-II (Tumor control): Animals were inoculated with 1x10^6 cells per mice intraperitoneal.
- Group-III (Standard Group): Animals were injected 5-fluorouracil (20mg/kg)intraperitoneal along with DAL cells 1x 10^6 cells per mice treatment.
- Group-IV (Test group–I): Animals were treated with aqueous alcoholic extract of *Cinnamomum malabatrum* (625mg/kg) orally along with DAL cells 1x 10^6 cells per mice treatment.
- Group-V (Test group-II): Animals were treated with aqueous extract of (500 mg/kg) *Cinnamomum malabatrum* orally along with DAL cells 1x 10^6 cells per mice treatment.

Effect of Alcoholic and Aqueous extract of stem bark of *Cinnamomum malabatrum* on mean survival time: Animals were inoculated with 1x 10^6 DEL cells per mouse on day 0^{th} and treatment with *Cinnamomum malabatrum* extract (both alcoholic and aqueous), were started 24hr after inoculation, at a dose of 625mg/kg per day, p.o. Alcoholic extract and 500mg/kg p.o. for aqueous extract. The control group was treated with the same volume of 0.9% sodium chloride solution, 5-fluorouracil at a dose of2 0mg.kg was used as standar ddrug. All the treatments were given for nine days. The mean survival time were for all groups was noted. The anti-tumor efficacy of *Cinnamomum malabatrum* was compared with that of tumor control. [31] The MST of the treated groups was compared with that of the control group using the following formula:

$$\text{Increase in lifespan}=T–C/Tx100$$

Where, C=no. of days control animals survived; T=no. of days the treated animals survived

Effect of Alcoholic and Aqueous extract of stem bark of *Cinnamomum malabatrum* on Haematological parameters: All the treatments were given for 9days on the 14day, all the animals were sacrificed under ether anesthesia and blood was drawn by retro orbital plexus method, WBC count, RBC count, hemoglobin, protein and packed cell volume were determined. Cells smear was prepared in slide and stained with Lieshman stain solution. Red blood cells (RBC), White blood cells (WBC) and Haemoglobin (Hb) were estimated with the help of hematology analyzer (Medonic CA620, Boule, Sweden). The RBC and WBC were expressed as 106 /mm^3 and 103/mm^3 of blood and Hb as g/dl of blood. [32, 33]

Effect of Alcoholic and Aqueous extract of stem bark of on different *Cinnamomum malabatrum* on solid tumor Simultaneous method: To determine the effect of Alcoholic and aqueous extract of *Cinnamomum malabatrum* on solid tumor, all the animals were injected with 1x10^6 cells/mouse in phosphate buffered saline into the right hind limb of all the animals simultaneously. All the treatments were started from the next day of inoculation and was continued for five alternative days. The measurement of tumor radii was taken from 11^{th} day of tumor induction and was repeated on every 5^{th} day for a period of 30 days. [34, 35] The volume of tumor mass was calculated from the formula:

$$V= 4/3\pi\ r^2$$

Where, r- is mean of r^1 and r^2 which are the two independent radii of the tumor mass.

Effect of Alcoholic and Aqueous extract of stem bark of *Cinnamomum malabatrum* on peritoneal cells in normal mice: One group of animals was treated with aqueous extract at a dose of 500mg/kg/day, p.o. of stem bark of *Cinnamomum malabatrum* once for a single day and the second group received the same treatment for two consecutive days. Similar treatment was given to other group with alcoholic extract at a dose of 625 mg/kg/day/p.o. the untreated first group was used as control. Peritoneal exudates of alcoholic and aqueous extract groups were collected after 24 hrand48hr of treatment by repeated intraperitoneal wash with normal saline (0.9%w/v) and the cells were counted in each of the treated groups under WBC newbauer‘s chamber and compared with those of normal control. [36]

Effect of Alcoholic and Aqueous extract of stembark of *Cinnamomum malabatrum* on body weight: Four groups of six mice each were transplanted intraperitoneal with $1x10^6$ Dalton‘s ascetic tumor cells. After 24h, the first and second group were orally treated with alcoholic and aqueous extract of *Cinnamomum malabatrum*. The third group, serving as the control, received normal saline (0.9% w/v). Treatments were continued for 9 days. Body weights were recorded every 5th day till 40 days of treatments or till the death of the animal.

Histopathological studies: A portion of liver, kidney and lungs of animals in all groups were stored in container for 12 hours in 10% formalin solution and subjected to histopathological studies by processing with paraffin embedding 5 micron section of the tissues stained with alum haematoxylin and eosin, were observed microscopically for histopathological changes. [37, 38]

STATISTICALANALYSIS: All the values were expressed as mean ± SEM (standard error of mean) for six mice, Statistical significance of difference between the control and experimental groups was assessed by one way ANOVA followed by Newman-Keuls Multiple Comparison test. The value of probability less than 5% ($P< 0.05$) was considered statically significant. [39, 40]

RESULTS AND DISCUSSION

Determination of extractive values of various extracts of stem bark of *Cinnamomum malabatrum*: The shade dried coarsely powdered stem bark of *Cinnamomum malabatrum* was extracted using different solvents of increasing polarity viz. Petroleum ether, Chloroform, Acetone and Ethanol by Continuous Hot Percolation method using Soxhlet

apparatus. The aqueous extract was prepared by cold maceration method. The extractive values are presented in Table 1.

Table 1: Data Showing the Extractive Values of *Cinnamomum malabatrum*

Plant name & Part used	**Methodof extraction**	**Extracts**	**Extractive Values (w/w)**
Cinnamomum malabatrum Stem Bark	Continuous Hot Percolation	Petroleum ether	1.92%
		Chloroform	1.68%
		Acetone	5.16%
		Ethanol	3.89%
		Aqueous	6.67%

Preliminary Phytochemical screening of various extracts of stem bark of *Cinnamomum malabatrum*: The phytoconstituents were identified by chemical tests, which showed the presence of various constituents in the different extracts. The results are shown in **Table 2**. The results shown that the alcoholic and aqueous extract of stembark of *Cinnamomum malabatrum* contain almost same and maximum number of pharmacologically active constituents. Hence both these extracts have been selected for the pharmacological studies.

Table 2: Data showing the Preliminary Phytochemical Screening for extracts of *Cinnamomum malabatrum*

Phytochemical constituents	**Petroleum ether**	**Chloroform**	**Acetone**	**Alcohol (95%)**	**Aqueous**
Alkaloids	-	-	-	-	-
Flavanoids	-	-	+	+	+
Carbohydrate	-	-	-	+	+
Saponins	-	-	-	+	+
Triterpens	+	-	+	+	-
Sterols	+	-	+	-	-
Tannins	-	-	+	+	+
Glycosides	-	-	-	-	-

+ve = Presence and -ve = Absent

Acute Toxicity Studies: The aim of performing acute toxicity studies is for establishing the therapeutic index of a particular drug and to ensure the safety in-vivo. Acute toxicity study is generally carried out for the determination of LD_{50} value in experimental animals. The LD_{50} determination was done in mice according to OECD guidelines by using Up and Down procedure and LD50 of alcoholic extract of stem bark of *Cinnamomum malabatrum* was found to be 625 mg/kg and the LD_{50} value of aqueous extract was found to be 500 mg/kg. The results of acute toxicity studies and data's were shown in **Table 3** and **4**.

Table 3: LD_{50} value of Alcoholic extract of *Cinnamomum malabatrum*

Group	Dose(mg/kg)	Dose difference	Dead
1	6000	-	0
2.	6100	100	0
3.	6200	100	1
4.	6300	100	1
5.	6250	50	1

LD_{50} value =6250 mg/kg ED_{50} value=625mg /kg

Table 4: LD50 value of Aqueous Extract of *Cinnamomum malabatrum*

Group	Dose (mg/kg)	Dose difference	Dead
1	4400	-	0
2.	4600	200	0
3.	4800	200	0
4.	5000	200	1
5.	4900	100	0

LD_{50} value =5000 mg/kg; ED_{50} value=500 mg/kg

Determination of effect of alcoholic and aqueous extracts of stem bark of *Cinnamomum malabatrum* on Mean survival Time: The effect of Alcoholic and Aqueous extracts of stem bark of *Cinnamomum malabatrum* on the survival time of the tumor bearing mice is shown in **Table 5**. The MST for the tumor control group was 20.83±0.47 days for aqueous (500 mg/kg/day p.o.) extracts treated groups. The MST of 5- fluorouracil (200mg/ kg i.p) treated group was 44.33± 0.49. The life span of animals treated with the alcoholic and aqueous extracts of stem bark of *Cinnamomum malabatrum* was significantly increased when

compared to untreated tumor bearing mice. The MST for Alcoholic extract treated group was increased to 40.75% and of aqueous treated group increased to 42.93%.

The reliable criterion for judging the value of any anti cancer drug is the prolongation of life span of the animals and disappearance of leukemia cells from blood. The results demonstrated the antitumor effect of alcoholic and Aqueous extracts of stem bark of *Cinnamomum malabatrum* against DAL cells in Swiss albino mice.

Table 5: Effect of Alcoholic and Aqueous extracts of stem bark of *Cinnamomum malabatrum* on Mean survival Time

Group	Treatment	MST (in days)	Increase in lifespan
I	Normal Control	-	-
II	Tumor control	20.83 ± 0.47	-
III	Standard group	44.33 ± 0.49	53.01
IV	Test group–I	35.16 ± 0.30	40.75
V	Test group- II	36.50 ± 0.42	42.93

Values are represented as mean ± S.E.M (n=6); One-way ANOVA followed by Student-Newman-Keulspost test ($P<0.001$).

Effect of Alcoholic and Aqueous extracts of stem bark of *Cinnamomum malabatrum*on Hematological Parameters: The Effect of alcoholic and aqueous extracts of stem bark of *Cinnamomum malabatrum* on hematological parameters of tumor bearing mice. Hematological parameters of tumor bearing mice on day 14 showed significant changes when compared to normal mice. The tumor bearing mice shows decreased level of hemoglobin, Red Blood Cells, Lymphocytes and increased level of White Blood Cells, Total Protein, Packed Cell Volume and Neutrophils. The treatment with alcoholic and aqueous extracts of stem bark of *Cinnamomum malabatrum* significantly altered all parameter, near to normal. Maximum alteration of parameters occurred in the group treated with the aqueous extract at the dose of 500 mg/kg/day p.o. fourteen days after transplantation, alcoholic and aqueous extract treated group were able to reverse the changes in the hematological parameter's consequents to tumor inoculation.

Effect of Alcoholic and Aqueous extracts of stem bark of *Cinnamomum malabatrum* on Solid Tumor Volume: The extract of *Cinnamomum malabatrum* showed remarkable reduction in solid tumor size. Tumor bearing mice shows significantly increased tumor volume viz. 15th, 20th, 25th and 30th day respectively. The tumor volume of control animals on 30th day was 11.66 ±0.33 ml, whereas it was 8.1± 0.25 ml ($p<0.001$)for Alcoholic (625 mg.kg/day/p.o) and 7.5 ± 0.34ml ($P<0.001$) for aqueous extract treated animals. The standard group animals treated with 5-fluorouracil shown tumor volume of 3.6± 0.21 ml ($P<0.001$). The maximum inhibition of tumor volume was produced by the aqueous extract at a dose of 500 mg/kg/day p.o. and maybe due to cytotoxic effect on DAL cells. The diminution of tumor size indicates the antitumor activity of *Cinnamomum malabatrum* **Table 6**.

Table 6: Data showing the Effect of *Cinnamomum malabatrum* on Solid tumor volume

Groups	**Treatment**	**Solid Tumor Volume (ml)**			
		15thdays	**20thdays**	**25thdays**	**30thdays**
II	Tumor Control	7.56 ± 0.22	8.16 ± 0.25	8.96 ± 0.25	11.16 ± 0.33
III	Standard Group	4.56 ± 0.22*	4.16 ± 0.21*	4.16 ± 0.25*	3.16 ± 0.21*
IV	Test Group-I	6.16 ± 0.25*	6.66 ± 0.22*	7.16 ± 0.22*	7.6 ± 0.25*
V	Test Group–II	5.56 ± 0.22*	6.33 ± 0.21*	7.33 ± 0.21*	8.1 ± 0.34*

Values are represented as mean ± S.E.M (n=6). One-way ANOVA followed by Student-Newman-Keuls post test ($P< 0.001$) is used. a-vs group I and b-vs group II.

Effect of Alcoholic and Aqueous extracts of stem bark of *Cinnamomum malabatrum* on peritoneal cell count: The average number of peritoneal exudates cells per normal mouse was found to be 5.8±0.01 x 10^6. Single treatment of Alcoholic extract of *Cinnamomum malabatrum* (625 mg/kg p.o.) enhanced the number to 7.21±0.6 x10^6 ($P<0.001$) and consecutive treatment for two days increase it to 10.21±0.06 x10^6 ($P<0.001$).Similarly single treatment with aqueous extract (500 mg/kg/day, i.p.) enhanced the count to 9.38±0.12 x10^6 ($P<0.001$) and consecutive treatment for two days increased it to 14.31 ±0.19 x10^6 ($P<0.001$). The result were shown in **Table 7**. To evaluate whether alcoholic and aqueous extracts of *Cinnamomum malabatrum* treatment indirectly inhibited tumor cell growth, the effect was determined on the peritoneal exudates cells of normal mice. Normally each mouse contains about 5x10^6 peritoneal cells, 50% of which are macrophages. Effect of alcoholic and aqueous extracts of stem bark of *Cinnamomum malabatrum* on DAL cells, probably mediated through

the enhancement and activation of macrophages or through some cytokine production inside the peritoneal cavity.

Table 7: Data showing the Effect of *Cinnamomum malabatrum* on Peritoneal Cell Count

Groups	Treatment	Peritoneal cell count ($1X10^6$)
I	Normal Control	5.08 ± 0.01
II	Tumor Control	3.21 ± 0.07 ***
III	Standard	10.21 ± 0.02 ***
IV	Test Group–I	9.48 ± 0.13**
V	Test Group-II	14.21 ± 0.12

*P<0.01; Values are represented as mean ± S.E.M (n=6).

Effect of Alcoholic and Aqueous extracts of stembark of *Cinnamomum malabatrum* on body weight of mice: The effect of extract of *Cinnamomum malabatrum* on average body weight of tumor bearing mice was also studied. The results are shown on **Table 8**. The average weight gain of tumor bearing mice on 20th day was 50.8±0.65. Normal animals showed a weight gain of 31.83± 0.83 on 35th day. The animals treated with 5-flurouracil shown an average body weight of 32.83± 0.47 on 35th day. The animal treated with the alcoholic and aqueous extracts of stem bark of *Cinnamomum malabatrum* shown average body weight of 37.33±0.33 (P<0.001 Vs standard) and 35.83±0.30 (P<0.001Vs standard) respectively on the 35th day.

Table 8: Data showing the Effect of *Cinnamomum malabatrum* on Peritoneal Body Weight

Groups	Treatment	Bodyweight			
		15thdays	20thdays	25thdays	30thdays
I	Normal Control	22.0 ± 0.72	23.0 ± 0.5	24.16 ± 0.54	27.16 ± 0.33
II	Tumor Control	27.85± 0.72a	40.16 ± 0.71	50.16 ± 0.65	54.16± 0.61
III	Standard	25.16 ± 0.25	30.66 ± 0.22	32.16 ± 0.66	35.6 ± 0.55*
IV	Test Group–I	25.56 ± 0.22	30.65 ± 0.31	32 ± 0.66	34.67 ± 0.34
V	Test Group–II	24.33 ± 0.32	29.56 ± 0.76	30.56 ± 0.88	31.56 ± 0.25
I	Normal Control	22.0 ± 0.72	23.0 ± 0.5	24.16 ± 0.54	27.16 ± 0.33

Histopathological Studies: Microscopically examination of liver section of normal control group showed normal arrangement of hepatocytes. Microscopically examination of liver section of tumor control group showed various degree of changes such as formation of steatoses, centrilobular fatty degeneration, cloudy swelling and necrosis of hepatic cells. Microscopically examination of liver section of mice treated with alcoholic extract of *Cinnamomum malabatrum* (625 mg/kg, p.o) showed some minor effects with little disarrangement of hepatic cell, fatty degeneration. The changes were mostly reversible. Remarkable improvement was noted in aqueous extract (500mg/kg, p.o) treated group. It showed little damage to liver cells with centrilobular fatty degeneration and reduced degree of vascularisation Microscopically examination of kidneys of normal mice showed normal morphological features of cells. The sections of tumor control group showed abnormal nuclei. The group treated with 5-FU(20 mg/kg, i.p) showed almost normal kidney section. The group treated with alcoholic (625 mg/kg, p.o) and aqueous (500 mg/kg, p.o.) extracts of *Cinnamomum malabatrum* showed decreased damage to kidneys. Microscopically examination of lungs showed normal arrangement of alveoli. The sections from tumor control group showed broadening of alveolar septa, damaged alveoli and infiltration of monocytes into the lungs. The groups treated with 5-FU (20mg/kg, i.p) shown almost normal lungs. The lung sections from mice treated with alcoholic (625mg/kg, p.o) and aqueous (500 mg/kg, p.o) extracts of *Cinnamomum malabatrum* showed less infiltration and alveolar damage.

CONCLUSION

Cinnamomum malabatrum ethanol and aqueous exhibits high anti-cancer activity against the cancer cell line. In general, the anti-cancer activities of the aqueous and ethanolextracts can be attributed to the presence of flavonoids, triterpenes and phenolic constituents, as well as other constituents reported in literature. The findings for this study provide a scientific rationale of using the plant to control cancer in traditional medicine. More validation studies are important to determine cytotoxicity of the extracts and optimal dosage of application in traditional medicine.

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