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EVALUATION OF ANTICANCER ACTIVITY OF CINNAMOMUM ZEYLANICUM AGAINST BLOOD CANCER CELL LINE

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ABSTRACT

Worldwide, leukemia is a major health concern. It ranks as one of the prevalent forms of cancer, particularly among children and adults. It affects individual of all age. The prevalence of leukemia varies geographically, with higher rates reported in developed countries where diagnostic capabilities and healthcare infrastructure are more advanced. The goal of present study was to calculate the antioxidant activity. The antiangiogenic activity was also performed using chick chorioallantoic membrane assay. Further, the decoction was evaluated against the leukemia cancer cell line K-562 for anti-cancer activity. The EC_{50} of DPPH (162.77±6.59%, p≤0.0001) and FRAP (133.65±6.00 mg) activity for *Cinnamomum zeylanicum* decoction was found to be higher as compared to standard (51.31±1.29% and 115.81±7.6 mg, respectively). The total phenol and flavonoid content of *Cinnamomum zeylanicum* decoction were 49.66±1.23 mg/GAE/100g and 12.67±0.03 mg/ RTE/ 100g, respectively. In the CAM assay, *Cinnamomum zeylanicum* decoction treatment shows less veins formation as compare to negative control. The *Cinnamomum zeylanicum* decoction treated group showed decrease in hemoglobin content than both the positive and negative controls. The decoction showed major anticancer activity against k 562 in contrast with Adriyamycin, a standard drug. The IC50 value observed for ADR was similar to cinnamon which is standard anti-cancer drug. Cinnamon was discovered to be the most potent cytotoxic agent, inhibiting K-562 cell proliferation by more than 50% at concentrations. Based on the study, we recommended the use of *Cinnamomum zeylanicum* as a possible remedy and preventative measure for cancer.

Keywords: Angiogenesis, Anti-cancer activity, *Cinnamomum zeylanicum*, Decoction, Leukemia cancer cell line

INTRODUCTION

Cancer is major threatening health issue amongst all disease throughout the world. The physiologically human body persistently produces a new cell which ultimately leads to repair damaged tissues. As per the natural phenomenon, cell proliferation and cell death occurred in defined form. In cancer disease, cell division, growth and death pattern is derailed. A tumor or an abnormal blood or lymph fluid in the body are the result of deregulation **(Schoene *et al.*, 2005)**. The blood related cancer known as leukemia that manifests as diffuse bone marrow invasion and altered pattern of hematopoietic progenitors. Acute lymphoblastic leukemia (ALL), acute myeloid leukemia (AML), chronic lymphocytic leukemia (CLL), and chronic myeloid leukemia (CML) are the four important types of blood cancer. Worldwidly, in 2020, leukemia was contributes around 2.5% and 3.1% of all new cancer incidences and associated mortality worldwide, respectively **(Sung *et al.*, 2020)**. Leukemia risk differs from population to population and was depends on several factors such as age, sex, and geography sites **(Lim *et al.*, 2014)**. These factors are may results in differences in the prevalence of various genetic as well as environmental risk factors for blood cancer **(Sathishkumar, *et al*, 2023)**. In India for the year 2023, projected number of cancer cases was found to be 1,496,972 individuals with a crude rate of 100.4 per 100,000 **(Sathishkumar *et al*, 2022)**. In 2024, according to other U.S. reports, approximately 2,001,140 new diagnosed cases of cancer will be detected and 611,720 individuals will die due to this disease **(Siegel *et al*, 2024)**. In India, around 26.7 million individuals were expected to have cancer in 2021 **(Kulothungan, *et al*, 2022)**.

Blood cancer in which impaired both blood cells as well as bone marrow also. Overall, it inhibits the bone marrow's potential to produce healthy red blood cells and platelets, appearing when the body produces an excessive amount of white blood cells **(Greim et al., 2015; Banerjee et al, 2023)**. There are two varieties of lymphoma: Hodgkin lymphoma and non-Hodgkin lymphoma, which both are origined from lymphocytes, which are white blood cells that help the body fight infections, while, Hodgkin lymphoma a type of cancer starts in lymphocytes that comprises the lymphatic system **(McCabe et al, 2015; Anand et al, 2022; Banerjee et al, 2023)**.

Secondary medicinal compounds are produced in small amount during plant metabolism and having molecular masses lesser than 3000 da **(Sanchez et al., 2000)**. Since 2600 BC, plant metabolites have been utilised, and following from last 4,000 years, secondary metabolites derived from plants were mostly used for food, medicine, and poisoning purposes **(Tsao et al., 2005)**. Plant secondary components have played a significant role, which indicated by considering that over 30% of pharmaceutical products get it directly or indirectly from natural sources **(Cragg et al, 2004; 2013; Nair et al, 2022)**. Pharmaceuticals, food additives, flavors, and other industrial materials mainly obtained from plant secondary metabolites by the utilization of plant cell cultures and it has solved a several issues **(Tiwari *et al*, 2015)**. For mankind used several secondary metabolites as flavorings, medicines, and recreational drugs traditionally **(Tiwari *et al.*, 2015)**. The plant secondary metabolites comprises of terpenes such as volatiles, carotenoids, sterols and glycosides; phenolics includes, coumarins, lignans, phenolic acids, stilbenes, flavonoids, tannins and lignin) and also nitrogen containing compounds like alkaloids and glucosinolates **(Mohiuddin *et al.*, 2019)**. Numerous studies have recently examined the health benefits of cinnamon in various diseases like Parkinsons **(Angelopoulou *et al.*, 2021)**, diabetes **(Khan *et al.*, 2003; Hasanzade *et al.*, 2013)**, blood purification **(Shirzad *et al.*, 2021)**, anti-inflammatory **(Kawatra and Rajagopalan, 2015; Shirzad *et al.*, 2021)** and cognitive function **(Kawatra *et al.*, 2015; Nakhaee *et al.*, 2024)**. Since its introduction of cinnamon as natural product, so many scientists' has been showed interest because of its several pleiotropic properties **(Kawatra *et al.*, 2015)**. Cinnamon may help to management blood glucose levels, according to several small randomized control trials **(Kawatra *et al.*, 2015)**. It has also been connected with a lowering the risk of heart diseases,which is the world's leading cause of deaths **(Leech, 2023)**. Moreover, sodium benzoate, a metabolite of cinnamon, increases the neurotropic factors like BDNF (brain-derived neurotropic factors) as well as neurotrophin-3 (NT-3) in the rodents central nervous system **(Rao *et al.*, 2014)**. The aqueous extract of cinnamon blocks the chemicals and pathways involved in cellular proliferation which associated with hematological malignancies including leukemia and lymphoma **(Caserta *et al.*, 2023)**. One of the most important and widely utilized spices in the world are the bark of several cinnamon species which are used in both traditional and contemporary medicine in addition to cooking **(Vangalapati *et al.*, 2012; Rao *et al.*, 2014)**. Because of its aroma, which is added to a wide range of foods, fragrances, and pharmaceutical items, cinnamon is mostly employed in the aroma and essence sectors **(Huang *et al*, 2007; Rao *et al*, 2014)**. The most vital elements of *cinnamon* are cinnamaldehyde and *trans*-cinnamaldehyde (Cin), which are contributed to the aroma and the different biological functions of cinnamon by being present in the essential oil **(Yeh *et al.*, 2013)**. According to research on *Cinnamomum*

osmophloeum (*C. osmophloeum*), there is a important amount of trans-cinnamaldehyde in the essential oil extracted from cinnamon leaves **(Chang *et al.*, 2008)**. Cinnamon exhibits several activities such as, antiallergenic **(Badger-Emeka *et al.*, 2020)**, anti-inflammatory **(Pagliari *et al.*, 2023)**, antiulcerogenic **(Tanaka *et al.*, 1989)**, antipyretic **(Mustaffa *et al.*, 2013; Arifullah *et al.*, 2014)**, antioxidant **(Kouassi *et al.*, 2015)**, anaesthetic activities **(Bedjaoui *et al.*, 2023)**, and antityrosinase activity **(Marongiu *et al*, 2007)**. Earlier antioxidant studies of bark of *Cinnamomum zeylanicum*, shown enhanced free radical scavenging ability against a variety of free radicals **(Marongiu *et al.*, 2007)**. The main chemical constituent which triggering this action is the cinnamonaldehyde **(Marongiu *et al.*, 2007)**.The goal of present study is to assess the antioxidant potential of *Cinnamomum zeylanicum* decoction. The antiangiogenic activity was also performed using chick chorioallantoic membrane assay. Further, the decoction was evaluated against the leukemia cancer cell line K-562 for its anti-cancer activity.

MATERIAL AND METHODS

Plant collection

The sticks of *Cinnamomum zeylanicum* were purchased from Ayurvedic practitioner, Satara, Maharashtra, India (Latitude 17.691401; Longitude 74.000938).

Decoction preparation

About 10gm cinnamon powder at 65℃ was added in 100ml distilled water and incubated for over the period of night with continuous shaking. Using Whatman filter paper no. 1 and a fine muslin cloth were used to filter the mixture. At 10,000 rpm for 15 min, filtrates were centrifuged and the clear supernatant was used for further tests, and the decoction was kept at 4°C **(Abubakar *et al.*, 2020)**.

Assessment of antioxidant activity

Estimation of 2,2-diphenyl-1-picrylhydrazyl (DPPH) scavenging assay

Diphenyl Picryl hydrazyl (DPPH) scavenging assay was performed as per the protocol describe by **Oyaziu (1986)**. Briefly, different concentrations (10, 20, 40, 60, 80, and 100 ug) of the cinnamon decoctions were taken in test tubes. Ascorbic acid (10-100 ug) was taken as a standard. To each tube, 5ml of 2**,**2- diphenyl-1-picrylhydrazyl (DPPH) reagent was added and mixed properly. Test tubes were kept at RT for 30 minutes in dark place. The absorbance was recorded at 517 nm in spectrophotometer (Shimadzu). The calculation of percentage scavenging activity was done by using following formula **(Mandave *et al.*, 2014)**.

$$\%\text{Scavenging} = [(OD_{control} - OD_{sample}) * OD_{control}] \text{ X } 100$$

Estimation of ferric reduction activity potential (FRAP) assay

Ferric reduction activity potential (FRAP) scavenging assay was performed as per the protocol describe by Chidambara *et al.* **(Chidambara *et al.*, 2002)**. Briefly, different concentrations (10, 20, 40, 60, 80, and 100) of the *cinnamon* decoctions were collected in the labeled test tubes. Then, 2.5 ml potassium ferricyanide (1%) and 2.5 ml phosphate buffer were added in the test tube. For 15 minutes, all tubes were incubated at 50°C. After that, 2.5 ml Trichloroacetic acid (TCA) and 0.5 ml $FeCl_3$ (0.1%) were added in the test tubes. In a spectrophotometer, absorbance was recorded at 700 nm. Ascorbic acid was tested and used as standard compound (10-100 ug) for further calculations **(Mandave *et al.*, 2014)**.

Assessment of phytochemical contents

Estimation of total phenol content (TPC)

Spectrophotometric analysis was performed to determine the concentration of phenolics present in cinnamon extract **(Singleton, 1999)**. Follin-ciocalteu assay method was used for the determination of the phenol content. Standard Guaiacol concentrations of 10, 20, 40, 60, 80, and 100 µg/ml were used. 2.8 ml of distilled water and 200 µl of the prepared decoction evolve the reaction mixture. 0.5 ml of the Follin-Ciocalteu reagent (1:1) was added after three minutes of incubation, 20% of sodium carbonate solution (2 ml) was added to the method. Test tubes were placed in a boiling water bath for one minute and then allowed to cool. The absorbance was recorded at 650 nm. The total phenol content was represented as equivalent of µg of guaicol **(Umdale *et al.*, 2021)**.

Estimation of total flavonoid content (TFC)

Total flavonoid content was estimated by using spectrophotometric method **(Kavirasan, 2007)**. The reaction mixture consists of 200 µl of decoction and 1.25 ml of distilled water was transferred to 10 ml test tubes. About 150 µl of 10% aluminum chloride was added and combined with 75 µl of 5% sodium nitrite after it had been prepared for six minutes. An ultraviolet visible spectrophotometer was used to measure the absorbance of the test and standard Rutin, a reference material, at 510 nm after five minutes **(Umdale *et al.*, 2021)**.

Estimation of tannin content

To determine the tannin content, folin-ciocalteu method was used **(Marinova, 2005)**. In a test tube, 7.5 ml distilled water and 0.5ml folin-ciocalteu phenol reagent was taken. Reference standard of gallic acid solution were estimated at 20, 40, 60, 80, and 100 µg/ml. In the reaction tube, 0.1ml of the sample decoction was added followed by the addition of 1 ml Na_2CO_3 (15%) solution to all tube. The mixture was shaken strongly and allowed to seat at room temperature for half an hour. Using a UV-visible spectrophotometer, absorbance at 750 nm was measured for test and standard solutions in relation to the blank.

Chick chorioallantoic membrane assay (CAM) assay

Hatchery was produced fertilized chicken egg. The egg was placed on the selected position on tray (Animal pole at the top). Eggs are incubated for 96 hrs (4 days) for the development of the CAM layer in incubator at 37°C. On 5th day, the eggs were taken out of incubator and kept in laminar air flow for further procedure. The eggs were randomly divided into three groups. The experimental groups are as follows.

Table 1 Experimental design

Sr. No.	Treatment group	Replicate
1	Negative control (Saline, 20 µl)	6
2	Positive control (Heparine, 20µl)	6
3	*Cinnamomum zeylanicum* decoction (20 µl)	6

The outer shell and inner thin shell membrane were removed with help of sterile pointed needle and forceps. The chorio allantoic membrane (CAM) layer was exposed for the further procedure. Whatsman filter paper disc (1 mm) (autoclaved) was carefully placed on the center of CAM layer with forceps. The treatment solution was administered on the filter paper disc which was placed on CAM as per given in the Table 1. The egg holes were sealed with white adhesive tape (parafilm). The eggs kept in the tray and incubated at 37°C for 16 day. For maintainace of humidity beaker filled with water was placed in incubator. Periodically eggs were rotated 3 times day. Observation of the development of veination was carried with help of light. Eggs are opened after developed embryo which shows complete veination, *i.e.*15-16th day. Photography was done to visualize the veination. The veination was also observed under light microscope (Olympus cx21i).

Hemoglobin estimation

Hemoglobin estimation was done as per the Sahli's method **(huang *et al.*, 2018)**. Briefly, hemoglobinometer tube was filled with HCl (1 N). In the Sahli's pipette, about 20 µl blood was drawn. The apparatus was stirred and wait for 10 min to hematin get settle down. Distilled water was added drop wise to mixture colour comparable to the comparator's standard glass. Percentage hemoglobin was estimated.

Estimation of anticancer activity against leukemia cancer cell line

Cinnamomum zeylanicum decoction's *in-vitro* anticancer activity was examined using the K-562 (leukemia cancer) cell line and the sulforhodamine-B (SRB) test method. K-562 was cultured in hydrated environment with 5% CO2 in the air at 37°C. The RPMI-1640 media fortified with 10% fetal bovine serum and 2 mM L-glutamine was used. The anti-tumor effects of adriyamycin (ADR) and cinnamonomum zeylanicum decoction were measured using an in vitro cytotoxicity assay based on sulphorhodamine B (SRB) against the K-562 cell line. The stock solution was continuously diluted to make different concentrations of the decoction of *Cinnamomum zeylanicum* and the positive control drug, adriyamycin, namely 10^{-7} M, 10^{-6} M, 10^{-5} M, and 10^{-4} M. The following process was used for the cell culture and SRB staining method (Pansare et al., 2016).
The GI50 (drug concentration needed for 50% reduction of cell growth as compare to untreated cells), TGI (drug concentration needed to reduce cell growth by 100% as compare to untreated cells), and LC50 (drug concentration needed to reduce cell growth by 50% of the initial cell number before drug incubation) values were measured.

Sulphorhodamine b (SRB) stanining

Sulphorhodamine B solution (50 µl, 0.4% w/v) added along with 1% acetic acid to each well and the plate was kept at room temperature for the 20 minutes. After staining, washing step was performed for five times with 1% acetic acid solution to remove residual dye. Then, plates were allowed to air dry. Afterward, 10 mM trizma base was used to wash out the bound stain and allowed to record absorbance by using ELISA plate reader at 540 nm, with 690 nm an reference wavelength.

Statistical analysis

All the experiment was performed thrice with three repeat in each. The data represented as mean ± standard error (SE). The Data were analyzed using one-way ANOVA followed by Dunnett Multiple comparison tests ($p<0.05$). Data analyzed by using GraphPad Prism and Instat (Version 5, GraphPad Software Inc., San Diego, CA, USA). For in vitro cell line study, assays were accomplished three times at different concentrations.

RESULTS

Plant collection and decoction preparation

Figure 1 represent *Cinnamomum zeylanicum* bark powder and extraction of secondary metabolites in the water by decoction method.

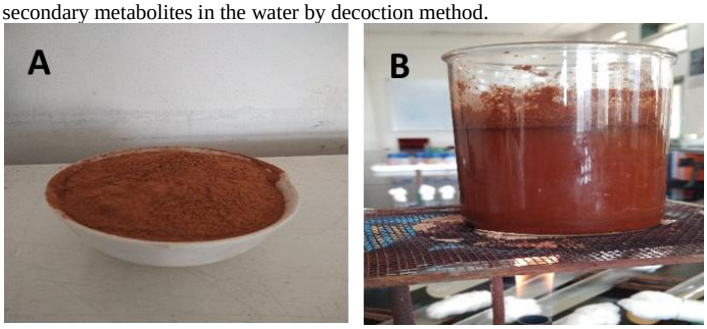

Figure 1 *Cinnamomum zeylanicum* bark powder and decoction decoction procedure**.** (A) *Cinnamomum zeylanicum* bark powder, (B) Aqueous extract by decoction method

Antioxidant activity

Table 2 represents the antioxidant activity of decoction of *Cinnamomum zeylanicum* and standard. The EC_{50} of DPPH activity for *Cinnamomum zeylanicum* (162.77 ± 6.59%) decoction was found to be significantly ($p\leq0.0001$) higher as compared to standard (51.31 ± 1.29%). The EC_{50} of ferric reduction antioxidant power assay (FRAP) of *Cinnamomum zeylanicum* (133.65 ± 6.00 mg) was non-significantly maximum as compared to standard (115.81 ± 7.6 mg).

Table 2 EC_{50} Antioxidant activity of *Cinnamomum zeylanicum*

Sr. No.	Assays	Standard	*Cinnamomum zeylanicum* decoction	p value
1	DPPH (%)	51.31 ± 1.29	162.77 ± 6.59	≤0.0001
2	FRAP (mg)	115.81 ± 7.6	133.65 ± 6.00	0.0699

The results are represented as mean ± SE (Standard Error). *DPPH:* Diphenyl picrylhydrazyl scavenging assay; FRAP: Ferric reduction activity potential scavenging assay; For DPPH EC_{50}: effective concentrations at which 50% inhibition are scavenged. For FRAP EC_{50}: 50% effective concentrations at which 0.5 absorbance recorded.

Quantitative estimation of phenolic and flavonoid content

Table 3 represents the total phenol content and total flavonoid content of *Cinnamomum zeylanicum* decoction. The total phenol and flavonoid content of *Cinnamomum zeylanicum* decoction were 49.66 ± 1.23 mg/GAE/100 g and 12.67 ± 0.03 mg/100 g RTE, respectively.

Table 3 Total phenol content and total flavonoid content of *Cinnamomum zeylanicum*

Sr No.	Assays	*Cinnamomum zeylanicum* decoction
1	Total phenol content (mg / GAE / 100 g ± SE)	49.66 ± 1.23
2	Total flavonoid content (mg / RTE / 100 g ± SE)	12.67 ± 0.03

The results are represented as mean ± Standard error. GAE: Galic acid equivalent; RTE: Rutin equivalent.

Chick chorioallantoic membrane assay (CAM) assay

Figure 2 represents the open eggs along with veination in CAM assay and its microscopic visualization. Negative control (A) showed more vein formation as compare to positive control (B). The treatment of *Cinnamomum zeylanicum* (C) decoction shows less veins formation as compare to negative control. Similar findings were observed in the Figure 2.

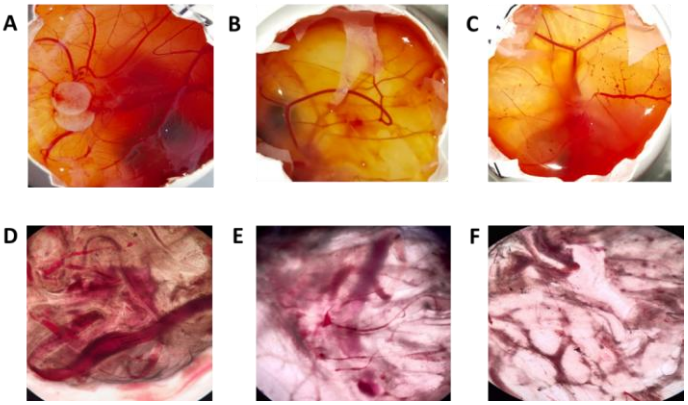

Figure 2 Visualization of CAM Assay *in vivo* and under microscope. A and D: Negative control (Saline); B and E: Positive control (Heparin); C and F: Treatment of *Cinnamomum zeylanicum* decoction

Hemoglobin estimation

Figure 3 represent the hemoglobin content in CAM assay. The hemoglobin content of positive control (heparin) and *Cinnamomum zeylanicum* decoction treated groups was found to be significantly ($p\leq0.001$) decrease in as compare to negative control.

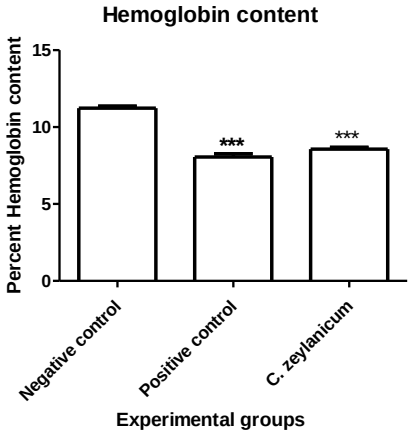

Figure 3 Hemoglobin estimation from CAM of experimental groups. The results are represented as mean ± SE (Standard Error). ***$p\leq0.001$ when compared with the control by Dunnett multiple Comparison Test.

Cinnamomum zeylanicum decoction showed inhibition of human leukemia (K-562) cell line

Anticancer activity of the *Cinnamomum zeylanicum* decoction against human leukemia cell line (K-562) was investigated *In vitro*. Table 4 summarizes the cytotoxicity data obtained by sulforhodamine-B (SRB) assay. Adriyamycin (ADR) was used as a standard control. Concentration 10^{-5} M showed minimum percentage as compare to other decoction concentrations. The GI_{50} value observed for *Cinnamon* was comparable with ADR which is a standard anti-cancer drug.

Table 4 Percentage control growth of human leukemia cell line K-562

Concentration	Standard control (Adriyamycin)	*Cinnamomum zeylanicum* decoction
10^{-4} M	23.23 ± 5.84	16.93 ± 1.68
10^{-5} M	22.3 ± 6.39	13.56 ± 1.66
10^{-6} M	30.66 ± 8.68	23.4 ± 0.90
10^{-7} M	29.63 ± 2.46	22.8 ± 5.46

The data is represented as mean ± standard deviation. The assay was performed in triplicate.

Generally, fifty percent growth inhibition (GI50) values were determined as the tested agents concentration showing 50% decrease of cell survival. From the obtained result, it can be depicted that the *Cinnamon* were most active cytotoxic agents which causing >50% inhibition of K-562 cell proliferation at concentrations 10^{-7} M, 10^{-6} M, 10^{-5} M and 10^{-4} M. The percentage control growth against molar drug concentration is depicted in the Figure 4.

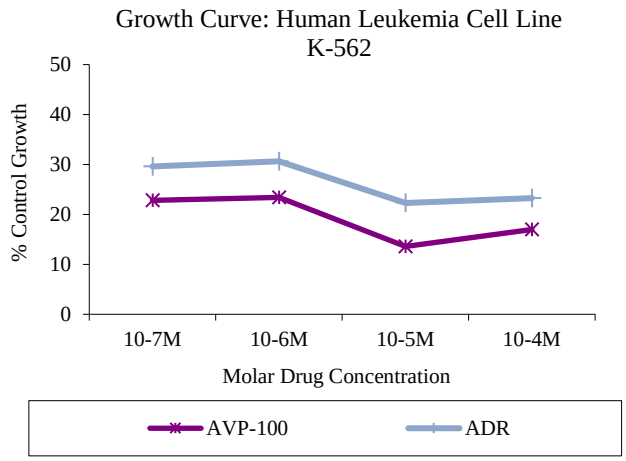

Figure 4 Human leukemia cell line K-562 growth curve. The data expressed as mean ± standard deviation. Molar drug concentration of 10^{-4}, 10^{-5}, 10^{-6}, 10^{-7} were used. *Cinnamomum zeylanicum* is more effective anti-cancer activity against K-562 as compared to Adriyamycin.

The TGI and LC_{50} values were found to be more than 100 in both Adriyamycin and *Cinnamomum zeylanicum* decoction treatment, respectively. GI_{50} was less than 0.1 in both above treatments. Drug concentrations (µMolar) calculated from Figure 4 and depicted in Table 5.

Table 5 Drug concentrations (µMolar) calculated from graph

Treatment	LC50	TGI	GI50*
Standard control (Adriyamycin)	>100	>100	<0.1
Cinnamomum zeylanicum decoction	>100	>100	<0.1

The results represented in Figure 4, Table 4 and 5 demonstrated that, Cinnamon have statistically high significant anti-cancer activity against K-562 in the comparison with Adriyamycin (ADR).

DISCUSSION

In the present study, we have used *Cinnamomum zeylanicum* decoction for estimation of phytochemical and antioxidant estimation, anti-angiogenic and anti-cancer activity. Various extracts of *Cinnamomum zeylanicum* was evaluated for their antioxidant activity reported by many authors **(Banglao *et al.*, 2020; Ashfaq *et al.*, 2021; Weerasekera *et al.*, 2021; Rakasivi and Chin, 2022)**. **Banglao *et al* (2020)** estimated antioxidant activity from cinnamon essential oils from *Cinnamomum zeylanicum*. He reported that the DPPH activity was ranges from 4.91 - 28.74% **(Banglao *et al.*, 2020)**. The present study,*Cinnamomum zeylanicm*decoction showed 162.77 ± 6.59 % DPPH radical scavenging activity. **Abeysekera *et al.*, (2019)** studied *Cinnamomum zeylanicum Blume* for its antioxidant activity and hyperglycemia regulatory properties. The antioxidant activity was found to be varied at diverse maturity stages of leaves. The mature bark showed maximum antioxidant activity as compare to other stages. **Wijewardhana *et al.*, (2019)** reported that *Cinnamon* bark extract showed highest total phenolic content among the sources taken. **Yang *et al.*, (2012)** reported that the total flavonoid contents were ranges from 0.031 - 3.348 g/ 100 g dry weight in various extracts of *Cinnamomum cassia*. However, in present study, *Cinnamomum zeylanicum* decoction showed 12.67 ± 0.03 mg/100g RT flavonoid content. Total phenol content of decoction of Cinnamomumzeylanicum were 49.66 ± 1.23 mg/GAE/100g.

Various reports are available for the use of medicinal plants for hematological malignancies **(Ferlazzo *et al.*, 2016; Mannucci *et al.*, 2018; Murdaca *et al.*, 2019; Innao *et al.*, 2021; Alesci *et al.*, 2022)**. Many oncology and hematologyclinicians stop the traditional drug and shifted towards the herbal / plant based alternatives **(Innao *et al.*, 2021; Alesci *et al.*, 2022)**. Different natural compounds were found to be effective against the inhibition and treatment of cancer **(Cirmi*et al.*, 2016; Tibullo *et al.*, 2016; Arlotta *et al.*, 2022; Allegra *et al.*, 2022; Ciceroet *al.*, 2022, 2023; Contino *et al.*, 2022; Vitalini *et al.*, 2022; Di-Salvo *et al.*, 2023)**. **Alimpoos*et al.*, (2018)** evaluated *Cinnamomum cebuense* for its antiangiogenic activity using CAM assay. *C. cebuense* leaf aqueous extract strongly hinder angiogenesis and thus prevent propagation and cancer cells metastasis. **Babar *et al* (2015)** reported that the *Cinnamomum cebuense* treatment (50% and 70% concentrations) significantly decrease the number of blood vessels during egg development. It also decreasesboth secondary and tertiary blood vessels formation. Our results are accordance with these reports. In the present study, *Cinnamomum zeylanicum* decoction treatement showed decrease in the vein formation as compare to negative control. Hemoglobin content was also found to be decrease as compare to negative control.

According to FAB classification, acute erythroblastic leukemia is refere to as M6 type of acute myeloid leukemias. The presence of K562 cells id a characteristic feature of it **(Al-Rawashde *et al.*, 2021; Weinberg and Arber, 2021; Tian *et al.*, 2022; Yu *et al.*, 2022)**. In the present study, we used K-562 cell line to evaluate the anti-cancer properties of *Cinnamomum zeylanicum* decoction. **Guan *et al.*, (2016)** reported that 50-75 µM cinnamon extract concentration (72 hr) was safe for K562 cells treatment. Sanyangxuedai, a key compound from cinnamon extract showed inhibition of K562 cells growth and found to be effective against treating leukemia. Aqueous cinnamon extract effectively inhibit leukemia and lymphoma of hematological malignancies **(Kwon *et al.*, 2010)**. The extract was effectively inhibite the molecules and pathways involved in cellular proliferation such as AP-1 and NF-KB. Downregulation of these molecules expression, further decrease in the correspondent RNA transcription and its protein. Also, it prevents the anti-apoptotic action of Bcl-2 in the cell **(Kwon *et al.*, 2010)**. In present study, *Cinnamon* has statistically significant anti-cancer activity against K-562 in the comparison with Adriyamycin which is standard anti-cancer drug. The IC50 value for *Cinnamon* decoction was comparable with Adriyamycin. These findings suggest that *Cinnamomum zeylanicum* could potentially serve as a complementary therapy alongside traditional treatments, which might help reduce the side effects associated with standard chemotherapy.

CONCLUSIONS

The study concluded that the water decoction of *Cinnamomum zeylanicum* effectively control blood cancer or effectively inhibit blood cancer cell proliferation. The result of current investigation stated that the *Cinnamomum zeylanicum* was found to be have maximum antioxidant activity. In CAM assay *Cinnamomum zeylaincum* decoction was found to be effective against angiogenesis. In CAM assay, maximum vein formation was observed in the vehicle control and *Cinnamomum zeylanicum* as compared to positive control. In microscopic visualization of blood veination shows more blood capillary network in positive control as compared to vehicle control. The decoction has reactive oxygen species neutralizing ability and composed of phenols and flovonoids as secondary metabolites. *Cinnamomum zeylanicum* exhibited anticancer activity against leukemia. Also, it effectively inhibits the angiogenesis, a key characteristic of cancer cells. Based on the study, we recommended the use of *Cinnamomum zeylanicum* as a prospective prophylactic and therapeutic agent against cancer treatment.

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