IJPSR (2021), Volume 12, Issue 1 **(Research Article)**

INTERNATIONAL JOURNAL OF PHARMACEUTICAL SCIENCES AND RESEARCH

Received on 21 January 2020; received in revised form, 10 June 2020; accepted, 15 June 2020; published 01 January 2021

PHYTOCHEMICAL INVESTIGATION, ANTIOXIDANT AND CYTOTOXIC ACTIVITY STUDIES OF ROOT BARK EXTRACTS OF *ARTOCARPUS HETEROPHYLLUS* LAM.

Shakkeela Yusuf [* 1, 2], Puthenkalam Melvin [1, 3], S. Reshma [1], Fathima Abdul Jaleel [1], P. R. Sreeja [1] and Jyoti Harindran [1]

Department of Pharmaceutical Sciences [1], Mahatma Gandhi University, Cheruvandoor Campus, Ettumanoor, Kottayam - 686631, Kerala, India.
Department of Pharmaceutical Chemistry [2], Unaizah College of Pharmacy, Qassim University, Saudi Arabia.
Churchill Hospital [3], OUH-NHS Trust, Old Road, Headington, Oxford, United Kingdom.

Keywords:

Artocarpus heterophyllus, DPPH, ABTS, MTT assay, HL60 Cell line, antioxidant, cytotoxic

Correspondence to Author:
Dr. Shakkeela Yusuf

Assistant Professor,
Department of Pharmaceutical Chemistry, Unaizah College of Pharmacy, Qassim University, Saudi Arabia.

E-mail: shakkeelayusuf@yahoo.com

ABSTRACT: Plant drugs enjoy much acclaim and worldwide acceptability even in the midst of amazing advancements in modern medicine. Current research in drug discovery from medicinal plants involves an approach combining botanical, phytochemical, and pharmacological techniques. In the present study, we selected the root bark of the plant *Artocarpus heterophyllus* Lam. belonging to the family *Moraceae*, to establish its phytochemical constituents, antioxidant property, and cytotoxic activity. Phytochemical evaluation of the total ethanolic extract (TEE) obtained showed the presence of alkaloids, glycosides, phenolic, flavonoids, amino acid, terpenoids, *etc*. The TEE was fractionated using solvents in the increasing order of polarity, i.e., petroleum ether, chloroform, and ethyl acetate. The antioxidant studies were conducted by DPPH and ABTS methods on chloroform extract (CE) and ethyl acetate extract (EAE) of the root bark of *A. heterophyllus* Lam. The extract which showed the greatest antioxidant property (EAE) was selected for cytotoxic studies using the MTT method on HL60 (Human promyelocytic leukemia) cell lines. Both the antioxidant and cytotoxic activity studies showed promising results.

INTRODUCTION: Consumption of plant-derived medicines is widespread and increasing significantly in both traditional and modern medicine. According to the World Health Organization, more than 80% of the world population in developing countries depends mainly on plant-based medicines for basic healthcare needs.

QUICK RESPONSE CODE

DOI: 10.13040/IJPSR.0975-8232.12(1).149-55

This article can be accessed online on www.ijpsr.com

DOI link: http://dx.doi.org/10.13040/IJPSR.0975-8232.12(1).149-55

A few of these genera *viz. Morus, Ficus,* and *Artocarpus* are economical sources of food and widely used in traditional medicine, agriculture, and industry. These genera received a great level of scientific interest as they contain medicinally important secondary metabolites possessing useful biological activities. Jackfruit and its pulp and seeds are rich sources of several high-value compounds with potential beneficial physiological activities [1].

The rich bioactive profile of jackfruit makes it a highly nutritious and desirable fruit crop. It is considered to be nutritious, cool, delicious, satisfying, and to prevent excessive formation of

bile, develop flesh, phlegm, strengthen the body and increase virility [2]. Research has offered ample evidence that routine dietary supplementation with jackfruit may protect against and even improve several disease conditions, including stomach ulcer and cardiovascular disease; it may even help to prevent and arrest the development of certain cancers, in addition to protecting the health of the mouth and skin [1] Moraceae is a large family comprising sixty genera and nearly 1400 species, including important groups such as *Artocarpus*, *Morus*, and Ficus [3]. *A. heterophyllus* or jackfruit (family of Moraceae*)* is a monoecious evergreen tree that is grown in several tropical countries[4]. *A. heterophyllus* is widely distributed in tropical region and has been used as traditional folk medicine against inflammation, malarial fever and so on. In addition, the function of *A. heterophyllus* in human health such as pulp and seed for tonic; root for diarrhea, fever; wood for muscular contraction; leaves for activating milk in women and animals, anti-syphilis, vermifuge, hypoglycaemic [5]. leaf ash for ulcers and wound. *Moraceae* plants, including *A. heterophyllus* are rich sources of isoprenylated phenolic compounds, including flavonoids. Jackfruit has diverse medicinal uses especially antioxidant, anti-inflammatory, antimicrobial, anti-cancer, and anti-fungal activity [6].

In our study, we selected the root bark of the plant *A. heterophyllus*, the total phenolics, and flavonoids of the root barks were evaluated [7]. The aim of this study was to establish the antioxidant property and cytotoxic activity of the extracts of root bark of the plant, which was not done before.

MATERIALS AND METHODS:

Collection and Authentication of Sample: Fresh roots of *A. heterophyllus* Lam, used for the study were collected from the outskirts of Kaduthuruthy village, Kottayam district, Kerala, India, during January 2017. The sample drug has been identified and authenticated by the botanist, Mr. Rogimon P Thomas, Assistant Professor, Department of Botany, CMS College Kottayam. A voucher specimen is preserved at CMS College Kottayam.

Extraction of *A. heterophyllus* Lam Root Bark: Shade dried the roots of *A. heterophyllus* Lam. Then the root barks were peeled off from the dried roots and powdered. The powder was soaked in ethanol (95%) in a round bottom flask overnight and was refluxed for 3 hours, and the solution was decanted off. The extraction was repeated thrice (or till colorless extract is obtained). All the extracts were combined and concentrated to a semisolid consistency. Thus, the total ethanolic extract was obtained. The fractionation of the ethanolic extract was carried out using solvents in the increasing order of polarity, *i.e.,* petroleum ether, chloroform, and ethyl acetate [8]. The yield for petroleum ether fraction was very less, so no further work was carried out on it. The other fractions were concentrated, weighed, and further studies were carried out.

Preliminary Phytochemical Evaluation: The total ethanolic extract was subjected to qualitative chemical analysis for the identification of various phytoconstituents. The phytochemical evaluation of the drug was carried out using standard procedures[8].

Antioxidant Assay:

DPPH Assay:

Principle: DPPH is α, α-Diphenyl, β-picryl-hydrazyl, long-lived organic nitrogen radical, and has a deep purple color. On accepting hydrogen from a corresponding donor, its solutions lose the characteristic deep purple color. The DPPH is a stable free radical and is widely used to assess the radical scavenging activity of antioxidant compounds. This method is based on the reduction of DPPH in methanol solution in the presence of a hydrogen donating antioxidant due to the formation of the nonradical form DPPH-H. This transformation results in a color change from purple to yellow, which is measured spectrophotometrically. The disappearance of the purple color is monitored at 517 nm [9].

2, 2-Diphenyl-1-picrylhydrazyl (DPPH) Assay:

Preparation of Standard Solution: The standard used was ascorbic acid. 100mg of ascorbic acid was taken in a100mg standard flask and made up the volume. From this, pipetted out 1ml into a 10 mL standard flask and made up the volume (stock solution). From this, pipetted out 1, 2, 4, 6, and 8 mL into different 10 mL standard flasks and made up the volume to obtain concentrations of 100, 200, 400, 600, and 800 µg/ mL, respectively [10].

Preparation of Test Sample: Stock solutions of samples were prepared by dissolving 10 mg of extract of each sample in 10 mL of ethanol to give a concentration of 1mg/ mL. From this, pipetted out 1 mL solution into a10 mL standard flask and made up the volume (stock solution). From this stock, solution pipetted 1, 2, 4, 6, and 8 mL into different 10 mL standard flasks and made up the volume with ethanol to obtain concentrations of 100, 200, 400, 600, and 800 µg/ mL, respectively.

Preparation of DPPH Solution: 2mL of ethanolic DPPH solution was added to 2mL of extracts and standard ascorbic acid at different concentrations 30 min later; the absorbance was read at 517 nm. Radical scavenging activity was calculated by the formula

Percentage inhibition = (absorbance of blank – sample/absorbance of blank) × 100

All the samples were assayed in triplicates and averaged. The concentration of the extract required to scavenge 50% of the radicles was calculated by plotting a graph of % inhibition *vs*. concentration.

ABTS Assay:

Principle: The peroxidase substrate 2,2'-azinobis (3-ethylbenzthiazoline-6-sulphonic acid) (ABTS), forming a relatively stable radical (ABTS•) upon one electron oxidation, has become a popular substrate for estimation of total antioxidant capacity. Kinetic assays, including the commercialized TAS assay (Randox), are based on the inhibition of the formation of ABTS• by one-electron oxidants. A simpler and more frequently applied approach is the decolorisation of preformed ABTS•. An obvious drawback of ABTS-based assays is the promiscuity of reactions of ABTS•, which is a non-physiological free radical. The preformed radical mono cation of 2,2'azinobis 3 ethyl benzo-thiazoline 6 sulfonic acid is generated by oxidation of ABTS with potassium persulfate (a blue chromogen) and is reduced in the presence of hydrogen donating antioxidants [11].

Procedure: The ABTS radical cation preparation: ABTS 2 mM (0.0548g in 50 mL) was prepared in distilled water. Potassium per sulphate 70 mM (0.0189 g in 1 mL) was prepared in distilled water. 200 µL of potassium per sulphate and 50 mL of ABTS were mixed and used after 2 h. This solution is called as ABTS radical cation, which was used for the assay. To the 0.5 mL of various concentrations of extract, 0.3 mL of ABTS radical cation and 1.7 mL of phosphate buffer, pH 7.4 was added. For control, instead of extract ethanol was taken. The absorbance was measured at 734 nm. The experiment was performed in triplicate.

Percentage inhibition was calculated using the following equation,

% Inhibition = (Avg. OD of control - Avg. OD of Test)/ Avg. OD of control × 100

***In-vitro* Cytotoxic Assay:**

MTT Assay: This is a colorimetric assay that measures the reduction of yellow 3-(4, 5-dimethythiazol-2-yl) -2,5-diphenyl tetrazolium bromide (MTT) by mitochondrial succinate dehydrogenase. The MTT enters the cells and passes into the mitochondria, where it is reduced to an insoluble, colored (dark purple) formazan product. The cells are then solubilized with an organic solvent (*e.g.,* isopropanol), and the released, solubilized formazan reagent is measured spectro-photometrically. Since, the reduction of MTT can only occur in metabolically active cells the level of activity is a measure of the viability of the cells. HL60 (Human promyelocytic leukemia) cell line was initially procured from National Centre for Cell Sciences (NCCS), Pune, India, and maintained Dulbecos modified Eagles medium (Gibco, Invitrogen).

The cell line was cultured in 25cm^2 tissue culture flask with DMEM supplemented with 10% FBS, L-glutamine, sodium bicarbonate and antibiotic solution containing: Penicillin (100U/ mL), Streptomycin (100µg/ mL), and Amphotericin B (2.5µg/ mL). Cultured cell lines were kept at 37ºC in a humidified 5% CO_2 incubator (NBS Eppendorf, Germany). The viability of cells was evaluated by direct observation of cells by an Inverted phase contrast microscope and followed by MTT assay method [12].

Cells Seeding in 96 Well Plate: Two days old confluent monolayer of cells were trypsinized, and the cells were suspended in 10% growth medium, 100µL cell suspension (5 × 10^4 cells/well) was seeded in 96 well tissue culture plate and incubated at 37 ºC in a humidified 5% CO_2 incubator.

Preparation of Compound Stock: The compound solution was filtered through 0.22 µm Millipore syringe filter to ensure sterility. After 24 hours the growth medium was removed, a freshly prepared compound in 5% DMEM was taken from this 6.25µg/ mL, 12.5µg/ mL, 25µg/ mL, 50µg/ mL, 100µg/ mL taken and makeup to 250µg/ mL using 5% MEM and were added in triplicates to the respective wells and incubated at 37 ºC in a humidified 5% CO_2 incubator [13]. The entire plate was observed after 24 h of incubation in an inverted phase-contrast tissue culture microscope (Olympus CKX41 with Optika Pro5 CCD camera), and microscopic observations were recorded as images. Any detectable changes in the morphology of the cells, such as rounding or shrinking of cells, granulation, and vacuolization in the cytoplasm of the cells, were considered as indicators of cytotoxicity.

Anti-proliferative Assay by MTT Method: To 15 mg of MTT (Sigma, M-5655) was reconstituted in 3 mL PBS until completely dissolved and sterilized by filter sterilization. After 24 h of the incubation period, the sample content in wells was removed, and 30µL of reconstituted MTT solution was added to all test and cell control wells; the plate was gently shaken well, then incubated at 37 ºC in a humidified 5% CO_2 incubator for 4 h. After the incubation period, the supernatant was removed, and 100µL of MTT Solubilisation Solution DMSO was added, and the wells were mixed gently by pipetting up and down in order to solubilize the formazan crystals. The absorbance values were measured by using a microplate reader at a wavelength of 540 nm.

The percentage of growth inhibition was calculated using the formula:

$$\% \text{ viability} = (\text{OD of Test}/ \text{OD of Control}) \times 100$$

RESULTS AND DISCUSSION: Preliminary phytochemical evaluation of the total ethanolic extract was subjected to qualitative chemical analysis for the identification of various phyto-constituents and revealed the presence of alkaloids, glycosides, phenolic, flavonoids, carbohydrate, proteins, amino acid, terpenoids, sterols, and saponins. In the DPPH assay, the percentage inhibition obtained for the different concentrations of sample extracts were compared to the percentage inhibition obtained with the standard as tabulated in **Table 1**.

TABLE 1: % INHIBITION BY STANDARD ASCORBIC ACID AND OF CE AND EAE OF *A. HETEROPHYLLUS* LAM. FOR DPPH ASSAY

Sample	Concentration (µg/mL)	Absorbance*	% Inhibition	IC_{50} (µg/mL)
Standard	100	0.312 ± 0.004	15.66	65.91
(ascorbic acid)	200	0.224 ± 0.007	39.42	
	400	0.197 ± 0.002	46.62	
	600	0.168 ± 0.005	54.63	
	800	0.095 ± 0.002	74.34	
CE	100	1.653 ± 0.06	0.99	113.5
	200	1.446 ± 0.04	13.37	
	400	1.274 ± 0.12	23.71	
	600	0.852 ± 0.12	48.94	
	800	0.819 ± 0.04	55.78	
EAE	100	0.234 ± 0.002	33.80	98.08
	200	0.121 ± 0.005	65.81	
	400	0.052 ± 0.0005	85.31	
	600	0.046 ± 0.0005	87.00	
	800	0.038 ± 0.0005	89.26	

*Values are expressed as mean ± SD, n = 3.

$DPPH^+$ scavenging property of CE and EAE in the range of concentration (100-800 (µg/mL)) and standard were tested, the extract showed a dose-dependent pattern in DPPH radical scavenging indicated by a decrease in purple color formation. IC_{50} value of the extract was found to be CE – 113.5 µg/mL, EAE- 98.08 µg/mL. The IC_{50} value of ascorbic acid was found to be 65.91 µg/mL. $DPPH^+$ radical scavenging activity of chloroform fraction, ethyl acetate fraction of *A. heterophyllus* is compared with standard ascorbic acid. Both the samples exhibited good $DPPH^+$ radical scavenging activity. When compared with that of the ascorbic acid (65.91(µg/mL)), EAE (98.08(µg/mL)) showed

a good result. Estimation of anti-oxidant activity by DPPH radical scavenging method showed that the ethyl acetate fraction and chloroform fraction had good antioxidant potential.

In ABTS antioxidant assay, the percentage inhibition obtained for different concentrations of sample extracts were compared to the percentage inhibition obtained with the standard and are tabulated in **Table 2**. $ABTS^+$, a protonated radical has the characteristic absorption maximum at 734nm, which decreases the scavenging of proton radical. In $ABTS^+$ cation radical scavenging method, the activity of tested extracts was expressed as a micromolar equivalent of an ascorbic acid solution having an antioxidant equivalent to 1g dry matter of the sample under the experimental investigation.

TABLE 2:% INHIBITION BY STANDARD ASCORBIC ACID AND OF CE AND EAE OF *A. HETEROPHYLLUS* FOR ABTS ASSAY

Sample	Concentration (µg/mL)	Absorbance*	% Inhibition	IC_{50} (µg/mL)
Standard	125	0.096 ± 0.0009	7.04	959.45
(ascorbic acid)	250	0.080 ± 0.0009	22.00	
	500	0.059 ± 0.0016	43.05	
	1000	0.037 ± 0.0009	64.09	
	2000	0.017 ± 0.0008	83.49	
CE	125	0.082 ± 0.0005	14.12	943.75
	250	0.058 ± 0.0005	39.22	
	500	0.054 ± 0.0007	42.88	
	1000	0.031 ± 0.0003	66.63	
	2000	0.031 ± 0.0005	67.57	
EAE	125	0.054 ± 0.0002	42.78	262.11
	250	0.048 ± 0.0005	49.68	
	500	0.037 ± 0.0003	60.98	
	1000	0.033 ± 0.0005	64.64	
	2000	0.016 ± 0.0007	83.05	

*Values are expressed as mean ± SD, n = 3

$ABTS^+$ radical scavenging activity of chloroform fraction and ethyl acetate fraction of *A. heterophyllus* is tabulated in **Table 2**. Both the samples exhibited good $ABTS^+$ radical scavenging activity. When compared with that of the ascorbic acid (959.45µg/mL), EAE (262.11 (µg/mL) showed excellent results. Estimation of antioxidant activity by ABTS radical scavenging method showed that the ethyl acetate fraction and chloroform fraction had excellent antioxidant potential. Phytocompounds related to flavonoids and phenolic acids found in *A. heterophyllus* root extract may have multiple biological and pharmacological activities, including antioxidative, cytotoxic, anticancer, antimicrobial, antiviral, and anti-inflammatory activities.

Antioxidants cause a protective effect by neutralizing free radicals, which are toxic by-products of natural cell metabolism. The human body has several mechanisms to counteract oxidative stress by producing antioxidants. These antioxidants act as free radical scavengers by preventing and repairing damages caused by reactive oxygen species and therefore, can enhance the immune defence and lower the risk of cancer and degenerative diseases [14].

The anti-proliferative activity of ethyl acetate fraction of *A. heterophyllus* was found out by MTT method on HL60 cell line. Cell viability was determined by means of the MTT reduction assay at the end of the incubation with sample EAE. The results were transformed to the percentage of control, and the IC_{50} values were graphically obtained from the dose-response curve.

As ethyl acetate fraction showed greater antioxidant potential than chloroform fraction, it was selected for determining its cytotoxic potential on HL60 cell line by MTT assay method. The IC_{50} value of ethyl acetate fraction on HL60 cell line by MTT assay method was found to be 35.524 µg/mL. Thus, the ethyl acetate fraction of *A. heterophyllus* has excellent potential as a cytotoxic agent on HL60 cell line. The phytochemical evaluation results in the various secondary metabolites like phenolic, flavonoids [15].

These secondary metabolites like phenolics and flavonoids have an important role as defence compounds. Phenolics exhibit several properties beneficial to humans, and their antioxidant properties are important in determining their role as protecting agents against free radical-mediated disease processes [16]. The ethyl acetate fraction also showed good antioxidant activity. The excellent cytotoxicity showed by the ethyl acetate fraction may be due to the presence cytotoxic composition available in fraction [17].

TABLE 3: % INHIBITION BY EAE OF *A. HETEROPHYLLUS* LAM. ON HL60 CELL LINE

Sample	Concentration (µg/mL)	Absorbance*	% Inhibition	IC_{50} (µg/mL)
Control	-	0.845 ± 0.0073	-	-
EAE	6.25	0.641 ± 0.0136	75.796	35.524
	12.5	0.453 ± 0.0086	53.570	
	25	0.423 ± 0.0120	50.082	
	50	0.293 ± 0.0031	34.672	
	100	0.247 ± 0.0085	29.300	

*Values are expressed as mean ± SD, n = 3

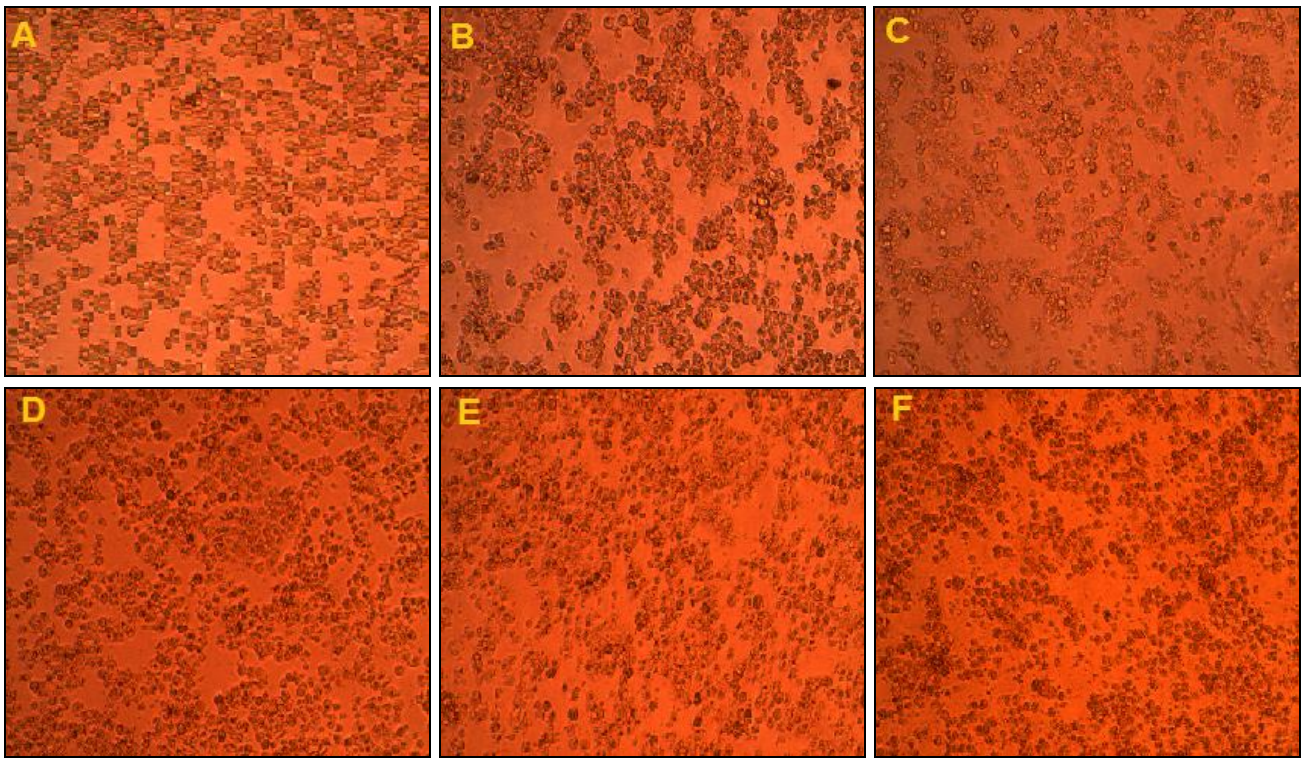

FIG: 1. EFFECT OF EAE ON HL60 CELLS USING MTT ASSAY. PHASE CONTRAST ANALYSIS OF CELL MORPHOLOGY (20X MAGNIFICATION). A- UNTREATED CONTROL CELLS SHOWING NORMAL MORPHOLOGY. B- CELLS TREATED WITH 6.25 µg/mL SIMILAR MORPHOLOGY AS THAT OF THE CONTROL CELLS SUGGESTING LITTLE TOXICITY, C- CELLS TREATED WITH 12.5 µg/mL DEPICTING MEMBRANE BLEBBING AND APOPTOTIC BODIES. D- CELLS TREATED WITH 25 µg/mL APOPTOTIC BODIES AND MEMBRANE BLEBBING DISTINCT, E- CELLS TREATED WITH 50 µg/mL PRESENCE OF DEAD CELLS AND MEMBRANE BLEBBING, SPINKOID CELLS AND APOPTOTIC BODIES DISTINCT. F- CELLS TREATED WITH 100 µg/mL BLEBBING, ECHINOID SPIKES

CONCLUSION: Dried root bark of *A. heterophyllus* Lam was selected for the study. In the present study, the extraction of dried root bark of *A. heterophyllus* Lam with ethanol was carried out. Then fractionated with petroleum ether, chloroform, and ethyl acetate. Antioxidant activity studies using DPPH and ABTS radical scavenging methods showed that the ethyl acetate fraction has excellent antioxidant activity and chloroform fraction has good antioxidant activity when compared with that of the standard ascorbic acid. Cytotoxic study conducted for the ethyl acetate fraction showed promising activity with HL60 cell line by MTT assay given the IC_{50} value of 35.524 µg/mL. Thus, the ethyl acetate fraction of *A. heterophyllus* has highly remarkable potential as a cytotoxic agent on the HL60 (Human promyelocytic leukemia) cell line. In the future, the

isolation of the active constituent responsible for the cytotoxic activity will be carried out.

ACKNOWLEDGEMENT: We express our gratitude to Biogenix Research Center, Kerala, India, for carrying out our work.

CONFLICTS OF INTEREST: The authors declare no conflict of interest

REFERENCES:

1. Swami SB, Thakor NJ, Haldankar PM and Kalse SB: Jackfruit and Its Many Functional Components as Related to Human Health: A Review. Compr Rev Food Sci Food Saf 2012; 11(6): 565-76.
2. Tyagi S. Medicinal uses of Jackfruit (*Artocarpus heterophyllus*). In: XII Agricultural Science Congress, ICAR, National diary Research Institute, Karnal, Haryana, India. 2015.
3. Patel RM and Patel SK: Cytotoxic activity of methanolic extract of artocarpus heterophyllus against a549, hela and mcf-7 cell lines. J Appl Pharm Sci 2011; 1(7): 167-71.
4. Ranasinghe RASN, Maduwanthi SDT and Marapana RAUJ: Nutritional and Health Benefits of Jackfruit (*Artocarpus heterophyllus* Lam.): A Review. Int J Food Sci. 2019; 1-12.
5. Chackrewarthy S and Thabrew MI: Hypoglycaemic and hypolipidaemic effects of an ethylacetate fraction of *Artocarpus heterophyllus* leaves. In: Glucose Tolerance. 2012; 207-22.
6. Vazhacharickal PJ, Mathew JJ, Kuriakose AC, Abraham B, Mathew RJ and Albin AN: Chemistry and medicinal properties of jackfruit (*Artocarpus heterophyllus*): a review on current status of knowledge. Int J Innov Res Rev 2015; 3(2): 83-95.
7. Yusuf S, Reshma S, Melvin P, Jaleel FA, Pr S and Harindran J: Estimation of secondary metabolites from the root bark extracts of *Artocarpus heterophyllus* Lams. Res J Pharm Biol Chem Sci 2018; 9(4): 766-72.
8. Kokate CK: PSBG. Pharmacognosy. 45th ed. Nirali Prakashan 2010: 108-09.
9. Mary LH, Lakshmi, Tilton F, Joseph J, Solosan S and Sudarsanam D: Phytochemical, antioxidant and cytotoxic properties of the fruit extract from *Cucurbita digitata*. Int J Pharm Pharm Sci 2014; 6(4): 353-6.
10. Yusuf and Shakkeela KKS: GC-MS analysis of oil isolated and antioxidant activity of *Shorea robusta* oleoresin. Am J Pharm Heal Res 2015; 3(11): 1-8.
11. Sivaraman A, Johnson M, Parimelazhagan T and Irudayaraj V: Evaluation of antioxidant potential of ethanolic extracts of selected species of Selaginella. 2013; 4(9): 238-44.
12. Arung ET, Wicaksono BD, Handoko YA, Kusuma IW, Yulia D and Sandra F: Anti-cancer properties of diethylether extract of wood from Sukun (*Artocarpus altilis*) in human breast cancer (T47D) cells. Trop J Pharm Res 2009; 8(4): 317-24.
13. Yusuf S, Srinivasan KK and Harindran J: Indigenous claim supports *in-vitro* antioxidant and cytotoxic screening of certain South Indian Medicinal Plants. J Pharm Biol Sci 2017; 12(3): 53-6.
14. Vijayalakshmi A, Kumar PR, Priyadarsini SS and Meenaxshi C: *In-vitro* antioxidant and anticancer activity of flavonoid fraction from the aerial parts of *Cissus quadrangularis* Linn. against Human Breast Carcinoma Cell Lines 2013; 1-9.
15. El-far AH, Oyinloye BE and Sepehrimanesh M: Date Palm (*Phoenix dactylifera*): Novel Findings and Future Directions for Food and Drug Discovery. 2018; 16(1): 2–10.
16. Saxena M, Saxena J, Nema R, Singh D and Gupta A: Phytochemistry of medicinal plants. J Pharmacogn Phytochem 2013; 1(6): 168-82.
17. Werdyani S, Wijayanti N, Fitria A and Rahmawati S: Cytotoxic effects of ethyl acetate fractions from secondary metabolites of Streptomyces Sp. GMY01 on human breast cancer MCF7 cell lines. Asian J Pharm Clin Res. 2017; 10(S. August): 9-11.

How to cite this article:
Yusuf S, Melvin P, Reshma S, Jaleel FA, Sreeja PR and Harindran J: Phytochemical investigation, antioxidant and cytotoxic activity studies of root bark extracts of *Artocarpus heterophyllus* Lam.. Int J Pharm Sci & Res 2021; 12(1): 149-55. doi: 10.13040/IJPSR.0975-8232.12(1).149-55.