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Review Article

TYPHONIUM FLAGELLIFORME: A MULTIPURPOSE PLANT

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ABSTRACT

Typhonium flagelliforme is a prominent plant candidate from aroid family, endowing various curative properties against a variety of illness and infections. This tropical plant found in damp, shady habitats and population of south east asian countries used it as alternative curative health supplement. Traditionally, this plant is used as a alternative remedy for cancer. Also, antibacterial and antioxidant activities are well established. This plant has shown promising results as a cough suppressant, which can be helpful in various respiratory tract problems. This review focuses on various biological activities of *Typhonium flagelliforme*.

Keywords: *Typhonium flagelliforme*, Anticancer, Antibacterial, Antioxidant, Chemical Constituents

INTRODUCTION

Herbs are staging a comeback and herbal 'renaissance' is happening all over the globe. The herbal medicines today symbolize safety in contrast to the synthetics that are regarded as unsafe to human and environment. The past two decades have seen a worldwide upsurge in the use of traditional medicine (TM) and complementary and alternative medicine (CAM) in both developed and developing countries. Although herbals had been priced for better compatibility with the human body, lesser side effects and better cultural acceptability, about 75–80% of the world population, showed interest and relies mainly on plants and plant extracts for their primary health care[1].

A plant from Malaysian lowlands got recent taxonomic and pharmacological attention[2]. *Typhonium flagelliforme* is an entire medicinal herb which belongs to the Araceae (Arum) family, commonly known as 'rodent tuber' in Malaysia. This plant grows widely in disturbed wastelands including soft, damp and shady habitats. And is native to the South East Asian countries and the southern part of India and Sri Lanka to Australia.[2, 3, 4].

Typhonium flagelliforme plant can grows up to 30 cm in height and has yellow coloured spadix enclosed in spathe, leaves are triangular in shape and tubers are whitish and oblong[3]. The spathe is 15.37 ± 1.17 cm long and 1.44 ± 0.07 cm broad at the widest portion. The spadix is divided into four portions: a lower 0.41±0.03 cm pistillate portion, an intermediate 1.48 ± 0.14 cm portion with sterile flowers, a 0.34 ± 0.05 cm staminate portion and terminated with lemon yellow 12.92 ± 1.25 cm rodent tail-like appendix [5].The distinguishing feature of araceae family which is bizarre combination of spathe and spadix which is useful in trappment of pollinators because of their particular morphology and organization of their inflorescences. Southern-east asian countries including India and China used this traditional plant from years for alternative cancer therapies. *Typhonium flagelliforme* is potential healthcare supplement to cure breast, lung, rectum, liver, prostate, pancreas and cervical cancers and leukemia's [2].

Being endowed with detumescence, detoxification, anti-inflammation, antivirus and anticancer bioactivities, plant is usually taken orally for treatment of cough, asthma and to soothe swelling of respiratory tract. To sweeten and increase patient acceptability, juice of the fresh whole plant is mixed with honey. Also, leaves are wrapped in longan flesh and taken raw [3, 6, 7, 8]. The flowers of *T. flagelliforme* have been used as anticoagulant by 'Filipinos' and Chinese used this plant as remedial for the treatment of injury[4]. Antibacterial and antioxidant activities of *T. flagelliforme* were reported in tuber extracts [6].

Chemical Constituents

In order to assess its phytochemical components, an experiment was conducted on one to six month old ex vitro and in vitro extracts of *T. flagelliforme.* The active (ex vitro and in vitro) extracts of *T. flagelliforme* were screened for phytochemicals components such as alkaloids, flavonoids, terpenoids and steroids. Alkaloids and flavonoids are the main phytochemical constituents of T. *flagelliforme* which are found to be in the highest amount in two and four month old of ex vitro plants. High amounts of main phytochemical constituents were observed during the flowering process which started in two month old plant and finished at the end of the three month old plant[5]. The other phytoconstituents include chain of saturated fatty acids like methyl esters of linoleic acid[9], hexadecanoic acid, octadecanoic acid, 9-octadecenoic acid and 9, 12-octadecadienoic acid. In addition, several common aliphatics were identified as dodecane, tridecane, tetradecane, pentadecane, hexadecane, heptadecane, octadecane, nonadecane and eicosane. None of the above identified compounds showed or are known to have cytotoxic behavior[2]. A variety of intercellular and extracellular enzymes also present in *T. flagelliforme* include peroxidase, laccase, tyrosinase, reductase, azo reductase, and riboflavin reductase[10]. Other include an acyclic diterpene alcohol, phytol and amino acids like arginine, tryptophan were also reported in different studies[11, 3]. In addition, phenylpropanoid glycosides, sterols and a cerebroside were also found in the root of this plant[2].

Therapeutic Activities of *Typhonium flagelliforme*

It is a medicinal herb which is endowed with curative properties against a variety of illness including injuries, oedema, pulmonary ailments and bleeding[5].

Anticancer Activity

Antiproliferative action

Typhonium flagelliforme have been reported to act as anticancer in a recent study conducted in Centre for Drug Research, University Sains Malaysia with School of Chemical Sciences, Malaysian Institute of Pharmaceuticals and Nutraceuticals, Ministry of Science Technology and Innovation collaboration by Choon-Sheen Lai et al. They investigated antiproliferative activity of plant in vitro on a human lung carcinoma cell line (NCI-H23) and a non-tumorigenic fibroblast cell line (BALB/c 3T3) using the bioactivity guided approach. For that, extracts of typhonium flagelliforme were fractioned by using flash column chromatography and each fraction was evaluated for antiproliferative activity using MTT assay. The apoptotic effect of the active fraction was determined microscopically and by using TUNEL colorimetric assay. GC–MS (Hyphenated gas chromatography and mass spectrometry) and NMR (^{1}H NMR) were used to determine the chemical constituents of this active fraction. Finally studies revealed that Several fractions of the hexane and dichloromethane extracts were found to inhibit the growth of NCI-H23 non-small cell lung carcinoma cell line significantly, with IC_{50} <15µg/ml (IC_{50} means half maximal inhibitory concentration). However most of these active fractions were also found to inhibit the growth of non-tumorigenic BALB/c 3T3 mouse fibroblast cell line except for fraction 21 of the dichloromethane extract (D/F21). This particular fraction was not only less cytotoxic to the non-tumorigenic cells where the IC_{50} was 48.6µg/ml compared to IC_{50} 7.5µg/ml for NCI-H23, but it was also found to induce apoptosis in the cancer cell line. GC–MS analysis revealed that D/F21 contains hexadecanoic acid, 1-hexadecene, phytol and a derivative of phytol. The presence of non-saturated fatty acids in this fraction was confirmed by nuclear magnetic resonance spectroscopy[3].

Cytotoxic activity

This plant was often included as an essential ingredient in various herbal remedies recommended for cancer therapies in Malaysia. Choo et al. performed an experiment which proved cytotoxic activity of *T. flagelliforme.* Experimentation methodology include testing of activity on murine P388 leukaemia cells using the MTT assay method. Various extracts prepared from either the roots, tubers, stems or leaves for research purpose. Both the chloroform (IC_{50} = 6.0 microg/mL) and hexane (IC_{50} = 15.0 microg/mL) extract from the 'roots and tubers' exhibited weak cytotoxic activity. The hexane extract (IC_{50} = 65.0 microg/mL) from the 'stems and leaves' exhibited weaker cytotoxic activity than the chloroform extract (IC_{50} = 8.0 microg/mL). Further analysis using an amino acid analyser revealed that the juice extract contained a high concentration of arginine (0.874%). A high tryptophan content (0.800%) was confirmed by NMR and HPLC analysis[11].

For cytotoxic action one more study was performed by Mohan et al, to investigate the potential *in vitro* cytotoxic effect of leaves and tubers of *T. flagelliforme* extracts against human T4-lymphoblastoid cell line CEM-ss. Only Dichloromethane and Ethyl acetate extracts of *T. flagelliforme* showed significant anti proliferative effect against CEM-ss cells, from eight extracts. Finally concluded that *T. flagelliforme* appears to be a promising plant demonstrating anti cancer activity [8].

Induction of Apoptosis

Induced by linoleic acid fraction of *Typhonium flagelliforme* in human T4 lymphoblastoid (CEMss)

A study was conducted by Syam Mohan et al which confirmed anti-leukemic activity by preparing *Typhonium flagelliforme* dichloromethane extract from tubers and tested on human T4 lymphoblastoid (CEMss) cell line. The dichloromethane (DCM) extract of tuber has been fractionated by column chromatography and evaluated for its cytotoxicity toward CEMss cells as well as human primary blood lymphocytes (PBLs). Phase-contrast Inverted Microscopy, SEM, TEM were used to assess Apoptosis and terminal deoxynucleotidyl transferase dUTP nick end labeling (TUNEL) assay was used for further confirmation of apoptosis. The data revealed that only few fractions showed significant cytotoxicity against the selected cell line CEMss, in which fractions DCM/F7, DCM/F11 and DCM/F12 showed exceptional activity. Further studies in the non-cancerous PBL (primary blood lymphocytes) exhibited significant selectivity of DCM/F7 compared to other fractions. Double-staining of acridine orange (AO)/propidium iodide (PI), SEM and TEM were collectively used to confirm cytological observations showed events like chromatin condensation, cell shrinkage, abnormalities of cristae, membrane blebbing, cytoplasmic extrusions and formation of apoptotic bodies. Results indicate that T. flagelliforme possess a valuable anti-leukemic effect and was able to produce distinctive morphological features of cell death that corresponds to apoptosis[2].

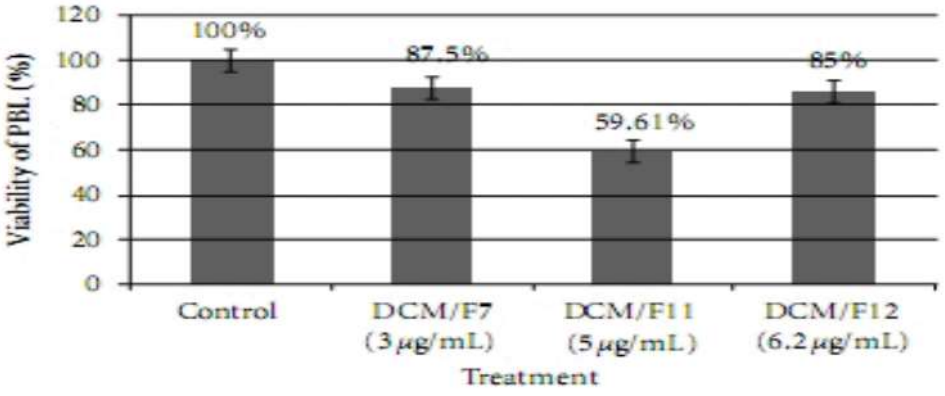

Figure 1: Inhibition effects of selected fraction (DCM/F7, DCM/F11 and DCM/F12) on proliferated human peripheral blood lymphocytes [2]

Apoptotic effect on murine leukemia WEHI-3 cells

This plant had shown to induce antiproliferative effect as well as apoptosis in cancer cells. Mohan et al. got success, when they investigate *in vitro* and *in vivo* effects of *Typhonium flagelliforme* on murine leukemia WEHI-3 cells. It was found that various extracts of *Typhonium flagelliforme* were used to detect *in vitro* inhibition of growth of leukemia cells. Only dichloromethane (DCM) tuber extracts had demonstrated apoptogenic effect when observed under fluorescent microscope. The results showed that the counts of immature granulocytes and monocytes were significantly decreased in peripheral blood of BALB/c leukemia mice after the oral administration of DCM tuber extracts of TF for 28 days with three doses (200, 400 and 800 mg/kg). These results were confirmed by observing the spleen histopathology and morphology of enlarged spleen and liver in leukemia mice when compared with the control. Furthermore, the cell death mechanism in the spleen tissue of treated mice was found via apoptosis[12]. Mechanistic approach from Syam Mohan et al revealed that activation of caspase-3 and-9, PARP cleavage and cytochrome C release were responsible for induction of apoptosis in CEMss cells[13].

Typhonium flagelliforme was not efficient to destroy every cell-line, an in-vitro cytotoxicity screening of the *Typhonium flagelliforme* extracts indicated high cytotoxicity effect on human lung carcinoma NCI-H23 cells and human mammary gland carcinoma T-47D cells, but the extracts were not active on human liver carcinoma HepG2 cells[14].

Antibacterial Activity

Both leaves and tubers of *Typhonium flagelliforme* exhibits antibacterial activity. Researchers used cold macerated extracts of solvents in the order of increasing polarity. The extraction was done for 7 days and evaluated. Finally, they found that only hexane extract shown anti bacterial activity against the selected strains. The hexane extract from *Typhonium flagelliforme* tuber had interesting activity against both the gram negative bacteria, *Pseudomonas aeruginosa* (11±1.0 mm diameter) and *Salmonella choleraesuis* (12±1.1 mm diameter). The positive control, Streptomycin had shown zone of inhibition of 20±1.5 mm, 20±1.3 mm, 23±1.5 mm and 23±1.0 mm in Methicillin Resistant *Staphylococcus aureus, Pseudomonas aeruginosa, Salmonella choleraesuis* and *Bacillus subtilis* respectively[6].

The same experiment was performed for *Typhonium flagelliforme* leaves using same conditions and leaves' hexane extract was capable to show antibacterial activity against *Pseudomonas aeruginosa* [7].

Antioxidant Activity

For testing the antioxidant activity, Researchers used two methods namely DPPH (2, 2-diphenyl-2-picrylhydrazyl hydrate) free radical scavenging and total phenolic compounds, were used for the antioxidant analysis. All the extracts were subjected to screening for their possible antioxidant activity. The DPPH assay showed that the inhibitory activity of ethyl acetate (77.6±0.9%) and dichloromethane (70.5±1.7%) extracts were having comparatively admirable inhibition capacity when compared to the positive control BHT (95.3±1.3%). Total phenolic content of all extracts was also evaluated, and dichloromethane extracts (5.21±0.82 GAE mg/g extract) was superior to all other extracts, followed by hexane (3.27±0.85 GAE mg/g) and ethyl acetate (2.49±0.33 GAE mg/g)(Mohan et. al, 2008). Above experiment was related with *Typhonium flagelliforme* tubers and same experiment was performed for *Typhonium flagelliforme* leaves using same conditions and results shows the Total phenolic content of Methanol extracts(5.69±0.15 GAE mg/g extract) was superior to all other extracts, followed by dichloromethane (5.31±0.82 GAE mg/g) and ethyl acetate (4.24±0.26 GAE mg/g)[6-7].

Seeing all above results *Typhonium flagelliforme* appears to be a promising plant demonstrating antibacterial and antioxidant activity that requires further investigation.

Miscellaneous Activities

Typhonium flagelliforme is plant with various pharmacological activities. Zhong et al performed an experiment in Guangxi Institute of Traditional Medical and Pharmaceutical Sciences, Nanning which shows that All the water, alcohol and ester extracts of *Typhonium flagelliforme* could significantly decrease cough times, increase phenol red outage in trachea, prolong asthma incubation period, decrease twisting times, inhibit ear swelling and decrease autonomic action times. Finally, they concluded that All water, alcohol and ester extracts of TFB have effects of relieving a cough, eliminating expectoration, antiasthmatic, analgesia, anti-inflammation and sedation[15].

CONCLUSION

Typhonium flagelliforme is a multipurpose plant having a great potential as anticancer, antioxidant, antibacterial and cough suppressant. In addition to being good candidate for acquiring various properties, efforts are being in process which can make it as new hope in therapeutics.

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