EXPLORATION & WONDERS OF MEDICINAL PLANT
“ASAFOETIDA” (HEENG) CONSTITUENT GALBANIC ACID
AS ANTICANCEROUS AND ANTIMUTAGENIC AGENT

Syed Sarah Abbas 1,2 | Safila Naveed 1 | Fatima Qamar 1 | Saba Javed Hussain 1 | Syed Hameez Jawed 2

1 Faculty of Pharmacy, Jinnah University for Women, Karachi, Pakistan.
2 Department of Pharmaceutics, Faculty of Pharmacy, University of Karachi, Pakistan.

ABSTRACT

Asafoetida is a oleo-gum resin, it is a dried latex obtained from roots and rhizomes by incision. Asafoetida is not only used as a culinary spice but also traditionally used to treat various diseases, including asthma, gastrointestinal disorders and intestinal parasites. This oleo-gum-resin possesses anti-fungal, anti-diabetic, anti-inflammatory, anti-mutagenic and antiviral, antispasmodic, antioxidant, antidiabetic, antimicrobial, antibacterial, antihemolytic, antiviral, antifungal, antitumoral, antileishmanial activities. There are various chemical compounds are found including sugars and polysulfides.[2] Asafoetida chiefly subsume resin (40-65%), gum (20-25%), and volatile oil (4-20%).[2]

The asafoetida comprises a number of sesquiterpenes of which assaresinotannol is the chief sesquiterpene. Asafoetida is also used as a flavoring agent and used as a constituent of many spice mixtures. Galbanic acid (GBA) is the active constituent present in the asafoetida having anti cancerous activity, it provide inhibitory effects on HIF-1 activation during hypoxia and normoxia. The investigation of galbanic acid (GBA) has done by fluorescence quenching, absorption spectroscopy, FT-IR, molecular docking and molecular dynamics (MD) simulation procedures.

OBJECT:
The main assessment of this review article is to emphasize the most latest and recent researches on anti cancerous effect of ASAFOETIDA (heeng), having different principle constituents responsible in treating the lethal diseases.

INTRODUCTION:

Ferula asafoetida belonging to family umbelliferae its plant is a tall perennial which grows up to 2 m and needs a dry moist soil. The dried latex and by making deep incision on the roots and rhizomes, an oleo-gum-resin, known as asafoetida is obtained.[1] Asafoetida is not only used as a culinary spice but also traditionally used to treat various diseases, including asthma, gastrointestinal disorders, intestinal parasites, etc. This oleo-gum-resin possess anti-fungal, anti-diabetic, anti-inflammatory, anti-mutagenic and antiviral actions. There are various chemical compounds are found including sugars and polysulfides.[2] Asafoetida chiefly subsume resin (40-65%), gum (20-25%), and volatile oil (4-20%).[2]

Asafoetida is used as a flavoring agent and used as a constituent of many spice mixtures. Galbanic acid (GBA) is the active constituent present in the asafoetida having anti cancerous activity, it provide inhibitory effects on HIF-1 activation during hypoxia and normoxia. The investigation of galbanic acid (GBA) has done by fluorescence quenching, absorption spectroscopy, FT-IR, molecular docking and molecular dynamics (MD) simulation procedures.

A different combination of asafoetida and GBA were used for their MDR reversal properties. When combined with very non-toxic concentrations of the sesquiterpene coumarins (50 μM) including umbelliprenin, farnesiferol B, farnesiferol C and lehmferin, proved significant MDR reversal activity of these coumarins.sesquiterpene coumarins decreases the P-glycoprotein-mediated multidrug resistance in MCF-7/Adr cancer cells.[17]

ROLE OF GALBANIC ACID

Galbanic acid (GA) is a biologically active sesquiterpene coumarin is obtained from ferula species. This compound demonstrates various biological properties including anticancer, cancer chemopreventive, anticoagulant, antiviral, and antileishmanial activities. GA can inhibit the growth of prostate cancer cells via decreasing androgen receptor abundance.[18] Two new sesquiterpene coumarins isolated from the plant Ferula narthex Boiss. narthexone and narthexol, with three coumarin derivatives, conferol, conferone and umbelliferone.[19]

MECHANISM TO TREAT CANCER:

Tumour reducing activity of eight commonly used spices in India was studied in mice transplanted intraperitoneally with Ehrlich ascites tumour. Oral administration of extracts of asafoetida could increase the percentage of life span in these mice by 64.7%, 52.9%, 47% and 41.1%.[21] Latest studies reflects that prolong apoptotic effect of GBA-SLNs (GBA-loaded solid lipid nanoparticles) compared with GBA may be due to the accumulation of GBA-SLNs in the tumor site because of deviant tumor pathology.[22] Recent research also shows that the human breast cancer mostly spread by The 4T1 cells tumor growth and metastatic pattern in BALB/c mice. Traditional folk medicine have been the most important source having a
anticancerous activity.[23]. The anti-proliferative activity was analyzed by BrdU assay.[24]BrdU can be incorporated into the newly synthesized DNA of replicating cells (during the S phase of the cell cycle) and substituting for thymidine during DNA replication. Antibodies specific for BrdU can then be used to detect the incorporated chemical and indicating cells that were actively replicating their DNA. Binding of the antibody requires denaturation of the DNA, usually by exposing the cells to acid or heat. Because it is neither radioactive nor myelotoxic at labeling concentrations, it is widely preferred for in vivo studies of cancer cell proliferation.[25] The resulting DNA-bound bromouracil moiety was subsequently detected by commercial anti-BrdU mAb without the need for a denaturation step.[26]

The exact mechanism of action of GBA still unclear but the present study revealed that the apoptotic mechanism of GBA was investigated mainly in H460 non-small cell lung carcinoma (NSCLC) cells because H460 cells were most susceptible to GBA than A549, PC-9 and HCC827 NSCLC cells. Galbanic acid showed cytotoxicity in wild EGFR type H460 and A549 cells better than other mutant type PC-9 and HCC827 NSCLC cells. Also, GBA significantly increased the number of Terminal deoxynucleotidyl transferase dUTP nick end labeling (TUNEL) positive cells and sub G1 population in H460 cells. Western blotting revealed that GBA cleaved poly (ADP-ribose) polymerase (PARP), activated Bax and caspase 9, attenuated the expression of Bcl-2, Bcl-xL, and Myeloid cell leukemia 1 (Mcl-1) in H460 cells. However, interestingly, overexpression of Mcl-1 blocked the ability of GBA to exert cytotoxicity, activate caspase9 and Bax, cleave PARP, and increase sub G1 accumulation in H460 cells. These findings suggest that GBA induces apoptosis in H460 cells via caspase activation and Mcl-1 inhibition in H460 cells as a potent anticancer agent for NSCLC treatment.[27]

MOLECULAR MECHANISM OF GALLBANIC ACID:

The molecular mechanism of galbanic acid (GBA) binding to matrix metalloproteinase 9 (MMP9) was investigated by fluorescence quenching, absorption spectroscopy, FT-IR, molecular docking and molecular dynamics (MD) simulation procedures. The fluorescence emission of MMP9 was quenched by GBA. The titration of MMP9 by various amount of GBA was also followed by UV–Vis absorption spectroscopy. The results also demonstrate that GBA, having a biologically active sesquiterpene coumarin derivative, has a strong ability to bind strongly to MMP9. Molecular docking results indicated that the main active binding site for GBA has been located in a hydrophobic cavity in the vicinity of Zn atom. Moreover, MD simulation procedure suggested that GBA as a sesquiterpene coumarin derivative can interact with MMP9, without producing any effect on secondary structure of MMP9.[28]

Some researches also shows that Ferula assa-foetida’s resin has an inhibitory effect on angiogenesis in chick chorioallantoic membrane. It seems that compounds of Ferula assa-foetida’s resin can be used to inhibitangiogenesis in cancer tissues.[29]

CONCLUSION:

In this review article we prominence the presence of Galbanic acid that is responsible to treat life threatening and lethal disease that usually caused the death of most of the individuals throughout the world.

REFERENCES:

2) Milad Iranshahy, Mehrdad Iranshahi, Traditional uses, phytochemistry and pharmacology of asafoetida (Ferula assa-foetida oleo-gum-resin)—A review, Journal of Ethnopharmacology, Volume 134, Issue 1, 8 March 2011, Pages 1–10


Poonam Mahendra and Shradha Bisht, Ferula asafoetida: Traditional uses and pharmacological activity, Pharmacognosy Reviews, 2012 Jul-Dec; 6(12): 141–146


Shumaila Bashir, Maahboob Alam, Achyut Adhikari, New antileishmanial sesquiterpene coumarins from Ferula narthex Boiss, Phytochemistry Letters, Volume 9, September 2014, Pages 46–50

Hoda Gudarzi, Mona Salimi, Saeed Irian, Amir Amanzadeh, Ethanolic extract of Ferula gummosa is cytotoxic against cancer cells by inducing apoptosis and cell cycle arrest, Natural Product Research: Formerly Natural Product Letters, Volume 29, Issue 6, 2015


22). Amir Hossein Mansourabadi, Ali Shams, Reza Mansourin, Effects of fennel, asafetida and ginseng ethanolic extracts on growth and proliferation of mouse breast cancer 4T1 cell lines, Advanced herbal medicine, Article 5, Volume 1, Issue 2, Spring 2015, Page 34-39


26). Morteza Eskandani, Jalal Abdolalizadeh, Hamed Hamishehkar, Galbanic acid inhibits HIF-1α expression via EGFR/HIF-1α pathway in cancer cells, Fitoterapia, Volume 101, March 2015, Pages 1–11


29). Seyed Damoon Sadoughi, Saide Zafar-Balanezhad, Javad Baharara, Investigating the effect of ethanolic extract of Ferula assa-foetida’s resin on angiogenesis in chick chorioalantoic membrane, RJMS 2015, 22(131): 80-87