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Pharmacokinetic and Bio-Distribution Study of Purified Fractions of Celery Extract in Rats

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Abstract

Introduction: The ethnic people cultures and traditions anywhere in the globe, ritual, legends, myths, folksongs, and medicinal practices.

Aim of the study: The main aim of the study is pharmacokinetic and bio-distribution study of purified fractions of celery extract in rats.

Material and method: The dosages of TA (Aq) and TA (Ethanol) that were used for the research were 2000 mg/kg at step 2 and repeat of 2000 mg/kg at step 2. Each day's dose of test material was formulated just before administration.

Conclusion: The results of the present study can be a useful lead for further investigation on SE, to evaluate the efficacy in management of Diabetes mellitus and its complications.

Keywords: Pharmacokinetic, Biodistribution study, Purified fractions, Celery extract, Medicinal Plants.

Introduction

1.1 Indian System of Medicine

The medical, therapeutic, and pharmaceutical components of Ayurveda are all well documented in texts written in Sanskrit and other Indian languages (Dev, 1999). Medical treatments, including as surgery and a kind of massage of vital energy points, are described in the Ayurvedic treatises known as the Samhitas, which may be traced back to the Vedas (Ebadi, 2007). The oldest written accounts of these plants are in the Vedic texts from the second millennium B.C., namely the Rig Veda and the Atharva Veda. The Charaka Samhita (900 B.C.) is the first known comprehensive book on Ayurvedic theory and practise; its major concern was with medicine. This book lays out all the cornerstones of Ayurveda, however it focuses mostly on digestion (which is called agni, or "internal fire"). The Susruta Samhita is another ancient text with an emphasis on surgery (Majumdar 1971; Krishnamurthy 1991). Most of the specific concepts of Ayurveda, including the

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dosha and subdosha, are laid forth in the AstangaHridayam, which was written about 500 A.D. (Grade 1954; Sharma 1979). The next major event occurred about 800–900 A.D. with the creation of the Madhava Nidana, the most well-known Ayurvedic treatise on illness diagnosis. According to Ayurveda, all substances (dravya) are combinations of the five elements (earth, water, fire, air, and space). The stuff might be anything, from live organisms to inanimate objects.

Traditional medicine has been a part of India's culture for thousands of years, with the Ayurvedic and Unani systems prospering (Surana et al., 2008). In addition to its status as an ethnomedicine, Ayurveda is recognised as a comprehensive medical system that addresses all aspects of human health. It emphasises finding common ground with the cosmos, as well as with nature and science. Because of its all-encompassing nature, this medical practise stands apart from others. According to this theory, a healthy lifestyle should be prioritised above other health concerns (Ravishankar and Shukla, 2007).

1.2 Role of Ethnobotany in Relation to Medicinal Plants

The ethnic people cultures and traditions anywhere in the globe, ritual, legends, myths, folksongs, and medicinal practices. There are lots of wild and cultivated plants play pivotal roles in the tribal culture and these relationships with plants have been maintained from generation after generation. Ethnobotanical It has been recognised since ancient times (Singh et al., 1994) that a wide variety of plants may be used to treat illness and promote wellness.

Systematic studies in Ethnobotany will give results of great value to the botanists, archaeologists, anthropologists, plant geographers, linguists, pharmacologists and phytochemists (Jain, 1997). It is very difficult to collect such valuable information from the ethnic groups or from tribal regions. In many cases the plants that are used in traditional medicines are location specific and deeply rooted in traditional, social, cultural, and religious values. Now the entire world has realized the value and importance of traditional medicines. So we should give priority for the conservation of medicinal plants. In addition to the conservation, we must avoid over exploitation of medicinal plants and also create awareness on the importance of cultivating rare endemic and endangered medicinal plants, utility of medicinal plants and preservation of germplasm.

1.3 Natural Product-Based Drug Discovery: History to Present Scenario

The history of natural product-based the antitumor agents taxol, vinblastine, vincristic, and doxorubicin, the immune-suppressants cyclosporine, and rapamycin, and the cholesterol lowering agent-statins are all examples of the remarkable success of drug discovery over the past century. The rational drug discovery from medicinal plants has been begun in the early of 19th century when morphine was first isolated in the year of 1806 from Paparversomniferum. Many bioactive phytochemicals viz. quinine, codeine, digitoxin, caffeine, salicylic acid, atropine, codeine, capsaicin, colchicine, cocaine etc. were subsequently isolated from medicinal plants in 20th century, which are still in use. Preceding World War II, a progression in the identification of pharmacologically active scaffolds from plants and microorganisms has been achieved. The antibiotics, such as penicillin, streptomycin etc. were isolated during that time. In the postwar epoch, new scaffolds namely reserpine from Rauwolfia serpentina, vinblastine from Catharanthus roseus, pilocarpine from Pilocarpus jaborandi, vancomycin from Amycolatopsisorientalis, erythromycin from Saccharopolyspora erythraea etc. were isolated. A total of 19 natural productbased drugs have been accepted for marketing globally between 2005 and 2010. Among them, 7 were classified as Two were medications generated directly from natural products, while ten were semisynthetic analogues of tiny compounds found in natural products. Several small compounds derived from natural products are now in various stages of clinical trials and may be selected as the medications in the future. In 2015, natural product-based drug discovery made significant progress with the Nobel Prize in physiology or medicine being given to William C. Campbell, Satoshi Omura, and Youyou Tu avermectins and artemisinin.

1.4 The Approaches of Plant Drug Research

Research into new medicines derived from plants requires a multidisciplinary strategy that integrates botanical, phytochemical, biological, and molecular methods. Plants are chosen species is a crucial step in plant-based drug discovery. Based on extensive ethnomedicinal survey followed by comprehensive literature review the plant species is chosen for drug discovery process. The selected plant is then collected and authenticated with the involvement of a Taxonomist. The plant is then extracted with suitable solvent, fractionated, and subjected to lead discovery process either employing bioassay guided fractionation or by random isolation of phytochemicals followed by preclinical assays. Finding a good lead is the first stage in the long process of developing a new medicine. The second stage of the drug discovery process is called "lead optimisation," and it makes use of both combinatorial and medicinal chemistry. Finally, the drug candidate is developed employing preclinical drug delivery, pharmacology, toxicology, pharmacokinetics evaluations. Finally, the drug candidate is subjected to clinical trial and approved molecule is a natural product-derived drug. A consideration attention is paid to find out the molecular mechanism involving different biological and molecular techniques in lead development process. A schematic flow of typical medicinal plant-based drug discovery has been depicted in figure 1.1. However, this drug discovery is very time consuming and complicated process as compared to the drug discovery from the library of synthetic agents. The process of natural product-based drug discovery requires more time as compared with synthetic drugs. However, the recent advancement in separation methods, spectroscopic techniques, robotic-based high throughput bioassays, and other biochemical analytical techniques will surely accelerate drug discovery process from medicinal plants. Molecular understanding has progressed, cell biology and genomics helps to identify different molecular targets in a disease pathogenesis. Therefore, it is now easier to design in vitro cell based or enzymatic assay for a particular target disease for further execution of high throughput bioassays for lead identification. Despite it is challenging to employ high throughput screening in natural product-based drug discovery, but techniques like HPLC bioactivity profiling via high throughput bioassays-microtiter plate technique hyphenated with capillary probe NMR ensures rapid lead identification from natural products.

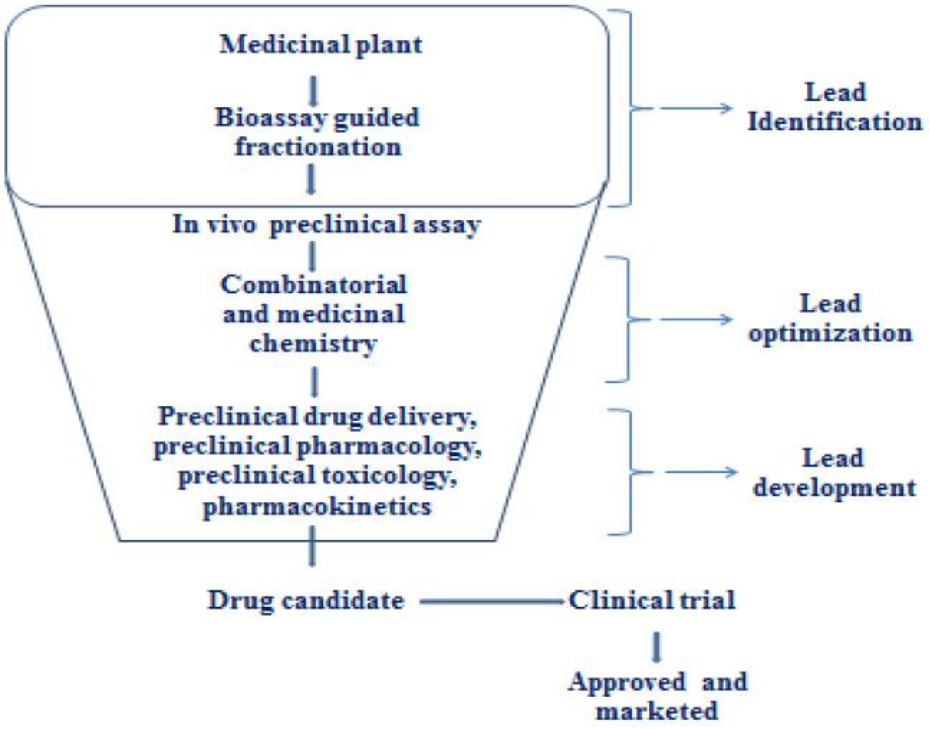

Figure 1.1. A schematic flow of generic approach of medicinal plant-based drug

Literature Review

Purohit *et al.* (2017) Three hundred fifteen adults from the Raika pastoralist group in several locations in Rajasthan, India, were surveyed to determine the current prevalence of PDM and DM. They discovered that the traditional Raika camel herders' prevalence of PDM and DM was highly impacted by demographic, nutritional, and lifestyle changes.

Tripathy *et al.* (2017) Researchers in the Indian state of Punjab looked at the incidence of diabetes and pre-diabetes among a stratified multistage sample of 5,127 residents. They discovered that 8.3% of the population had diabetes, and 6.9% has prediabetes. Diabetes mellitus was strongly connected to being between the ages of 45 and 69, being married, having high blood pressure, being overweight, and having a family history of the disease.

Swaroop *et al.* (2017) 225 pregnant women between 24 and 28 weeks of gestation who were seen at the antenatal OPD at UP RIMS & R in Saifai, Uttar Pradesh, India between January 2014 and January 2015 were included in the research. They discovered that 22 women (9.7%) were diagnosed with GDM, and that the presence of GDM was significantly associated with increased body mass index (BMI), birth weight, and newborn problems (P<0.05).

Kizilgul*et al.* (2017) drew the conclusion from their case study that celiac crisis is an extremely rapid and potentially fatal onset of celiac disease. Diagnosis was made based on diarrhoea, severe metabolic and electrolyte problems, and subsequent improvement with the introduction of a gluten-free diet in 3–8% of individuals with Type 1 DM.

Kidist*et al.* (2017) Institutional Cross-Sectional Study of Diabetic Complications and Risk Factors in Amhara Regional State, Ethiopia was carried out using a pre-tested questionnaire and a comprehensive assessment of relevant records. Complications among type 2 DM patients were shown to be common, with a frequency of 25.5% for retinopathy, 21.2% for diabetic foot ulcers, and 11.4% for diabetic nephropathy.

Methodology

3.1 Determination of Insulin Level and Calculation of Homa-IR and Homa-B

At 11 weeks post-treatment, insulin levels are measured using a radioimmunoassay. A blood sample taken when the subject is fasting and contains clot activator is placed in a red top tube. Before being sent to the pathology lab, all samples are kept at 4 degrees Celsius. At 11 weeks into therapy, fasting serum insulin and fasting plasma glucose levels are used in the following method with conversion factors to determine HOMA-IR and HOMA-β scores.

Insulin (1U/l = 7.174 pmol/l)

Blood glucose (1 mmol/l = 18 mg/dl).

HOMA-IR =[Insulin (U/l) × Blood glucose (mmol/l)]

$$\text{HOMA-}\beta = \frac{[20 \times \text{Insulin(U/l)}]}{[\text{Blood glucose(mmol/l)} - 3.5]}$$

3.2 PTP1B Inhibitory Activity *In Vitro*

The colorimetric PTP1B inhibition test kit is used. The concentration of the phosphate solution used to generate the phosphate concentration-time curve is between 0.25 and 3.0 nM. There are three separate runs of each experiment. The final concentration of extracts examined is between 1 and 400 ng/ml. The standard used is a suramin concentration of 1-100 ug/ml. Both the test and standard solutions are diluted 15 times in the phosphate buffer that comes with the kit.

3.3 Pharmacokinetic and Bio-Distribution Study of Purified Fractions of Celery Extract in Rats:

3.3.1 Dose Selection and Preparation:

- The client-provided sample was kept at room temperature.
- For both the TA (Aq) and TA (Ethanol) samples, the dosages used for the investigation were 300 mg/kg at the first step and repeated 300 mg/kg.
- The dosages of TA (Aq) and TA (Ethanol) that were used for the research were 2000 mg/kg at step 2 and repeat of 2000 mg/kg at step 2. Each day's dose of test material was formulated just before administration. Water was employed as the dosage preparation vehicle.

Results

4.1 Pharmacokinetic and Bio-Distribution Study of Purified Fractions of Celery Extract in Rats

4.1.1 Body weight data (gm)

Table 4.1 Step 1 (300 mg/kg)

Group	Ani.No	Sex	Marking	0 Day	07 Day	14 Day
TA (Aq)	**1**	**F**	**H**	101.0	127.0	147.0
	2	**F**	**B**	122.0	146.0	156.0
	3	**F**	**T**	109.0	138.0	154.0
Mean				**110.7**	**137.0**	**152.3**
SD				**10.6**	**9.5**	**4.7**
TA (Ethanol)	**4**	**F**	**HB**	120.0	142.0	168.0
	5	**F**	**BT**	111.0	130.0	148.0
	6	**F**	**HT**	102.0	122.0	145.0
Mean				**111.0**	**131.3**	**153.7**
SD				**9.0**	**10.1**	**12.5**

Table 4.2 Step 2 (300 mg/kg)

Group	Ani.No	Sex	Marking	0 Day	07 Day	14 Day
TA (Aq)	**1**	**F**	**H**	105.0	119.0	147.0
	2	**F**	**B**	120.0	141.0	150.0
	3	**F**	**T**	113.0	123.0	139.0
Mean				**112.7**	**127.7**	**145.3**
SD				**7.5**	**11.7**	**5.7**
TA (Ethanol)	**4**	**F**	**HB**	110.0	130.0	153.0
	5	**F**	**BT**	121.0	147.0	162.0
	6	**F**	**HT**	112.0	126.0	149.0
Mean				**114.3**	**134.3**	**154.7**
SD				**5.9**	**11.2**	**6.7**

Table 4.3 Step 3 (2000 mg/kg)

Group	Ani.No	Sex	Marking	0 Day	07 Day	14 Day
TA (Aq)	**1**	**F**	**H**	101.0	114.0	131.0
	2	**F**	**B**	137.0	151.0	171.0
	3	**F**	**T**	124.0	141.0	168.0
Mean				**120.7**	**135.3**	**156.7**
SD				**18.2**	**19.1**	**22.3**
TA (Ethanol)	**4**	**F**	**HB**	105.0	120.0	141.0
	5	**F**	**BT**	131.0	147.0	160.0
	6	**F**	**HT**	107.0	128.0	150.0
Mean				**114.3**	**131.7**	**150.3**
SD				**14.5**	**13.9**	**9.5**

Table 4.4 Step 4 (2000 mg/kg)

Group	Ani.No	Sex	Marking	0 Day	07 Day	14 Day
TA (Aq)	**1**	**F**	**H**	111.0	121.0	139.0
	2	**F**	**B**	117.0	131.0	150.0
	3	**F**	**T**	120.0	145.0	161.0
Mean				**116.0**	**132.3**	**150.0**
SD				**4.6**	**12.1**	**11.0**
TA (Ethanol)	**4**	**F**	**HB**	101.0	125.0	139.0
	5	**F**	**BT**	121.0	137.0	152.0
	6	**F**	**HT**	113.0	131.0	156.0
Mean				**111.7**	**131.0**	**149.0**
SD				**10.1**	**6.0**	**8.9**

Table 4.5 Summary of Results

	Step	Dose (mg/kg)	No. of Treated Rats	Terminal	Found Dead(X)
TA (Aq)	**1**	300	03	03	0
TA		300	03	03	0
TA (Aq)	**2**	300	03	03	0
TA		300	03	03	0
TA (Aq)	**3**	2000	03	03	0
TA		2000	03	03	0
TA (Aq)	**4**	2000	03	03	0
TA		2000	03	03	0
	TOTAL	-	**24**	**24**	**0**

4.2 Clinical Signs for Tamra Bhasma

Step I – 30.00 mg/ml: The test materials **TA (Aq) and TA (Ethanol) 3** caused **NO mortality**. No clinical indications of intoxication were seen in any of the animals during the course of the trial, and this held true for both single and multiple doses.

Step II – 200.00 mg/ml: The test materials **TA (Aq) and TA (Ethanol)** caused **NO mortality**. No clinical indications of intoxication were seen in any of the animals during the course of the trial, and this held true for both single and multiple doses.

Necropsy: During necropsy, we saw no overt pathological changes in any of the female rats given the test dosages.

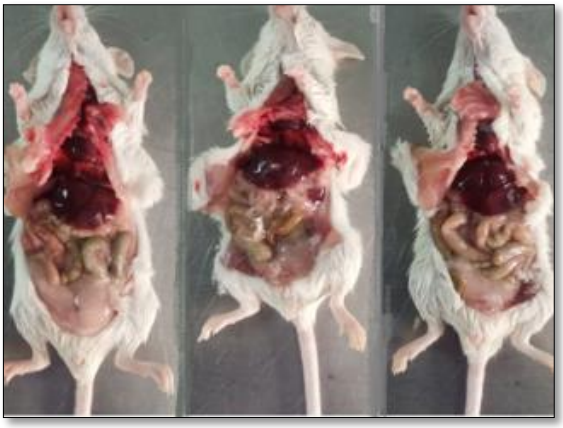

Figure 1Gross necropsy Step 1&2

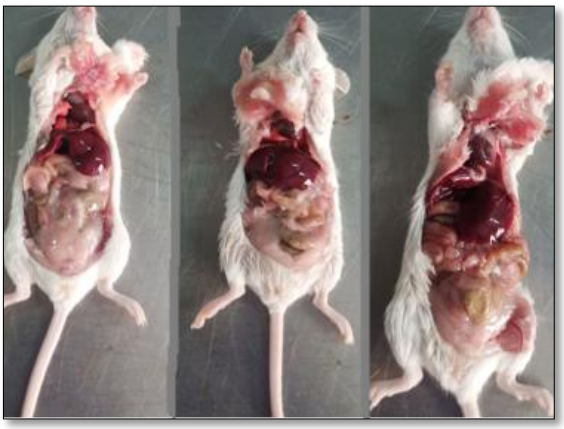

Figure 2: Gross necropsy Step 3&4

Conclusion

The results of the present study can be a useful lead for further investigation on SE, to evaluate the efficacy in management of Diabetes mellitus and its complications. The studies can be further directed for isolation and characterization of active constituents present in the seed and understanding of the underlying therapeutic processes that allow it to work. Studies may also be planned to assess usefulness and safety profile of the seed in preclinical and clinical settings.

SE also exhibited beneficial effects on cardiac functional parameters like, mean blood pressure, heart rate, hypertrophy indices, lipid levels, serum LDH and CK-MB levels, oxidative stress status and insulin resistance. This indicates that SE has results that favourably influence the prevention of diabetes-related cardiovascular problems. SE possess potent antioxidant action, which may be an important mechanism of its protective effect on diabetic complications. In addition to this, based on the PTP1B inhibitory activity of extracts, we can conclude that it has ability to reduce insulin resistance and increase glucose uptake in tissue. These effects may be on account of its diverse tannin and flavonoid contents. Apart from this, as discussed earlier, various chemical constituents present in SE have demonstrated varied actions like, insulin secretogogue, hypolipidemic, hypotensive, anti-inflammatory, analgesic, neuroprotective, TNF α inhibitory, COX inhibitory, prevention of AGE formation and beta cell protective actions, which all in combination may provide an overall protection against disease progression and development of complications as observed in our study. The current study's findings may provide a solid foundation for future research on SE, helping scientists determine the plant's usefulness in the treatment of diabetes and associated consequences. Research may also be focused on identifying the processes responsible for the plant's positive impact and isolating the active elements

responsible for those mechanisms. Preclinical and clinical studies might be planned to assess the plant's safety and effectiveness.

Limitations of the Study

- This study is limited to diabetes only.
- This study is limited to celery seeds only.

References

1. Ahmed, B., T. Alam, M. Varshney and S. A. Khan (2002). "Hepatoprotective activity of two plants belonging to the Apiaceae and the Euphorbiaceae family." Journal of Ethnopharmacology 79(3): 313-316.
2. Ahmed, S. S. S. J. and V. Ramakrishnan (2012). "Systems Biological Approach of Molecular Descriptors Connectivity: Optimal Descriptors for Oral Bioavailability Prediction." PLOS ONE 7(7): e40654.
3. Akbari, M. and V. Hassan-Zadeh (2018). "Hyperglycemia Affects the Expression of Inflammatory Genes in Peripheral Blood Mononuclear Cells of Patients with Type 2 Diabetes." Immunol Invest 47(7): 654-665.
4. Al-Asmari, A. K., M. T. Athar and S. G. Kadasah (2017). "An Updated Phytopharmacological Review on Medicinal Plant of Arab Region: Apium graveolens Linn." Pharmacognosy reviews 11(21): 13-18.
5. Al-Howiriny, T., A. Alsheikh, S. Alqasoumi, M. Al-Yahya, K. ElTahir and S. Rafatullah (2010). "Gastric antiulcer, antisecretory and cytoprotective properties of celery (Apium graveolens) in rats." Pharm Biol 48(7): 786-793.
6. Al-Sa'aidi, J., M. Alrodhan and K. Ismael (2012). "Antioxidant activity of n-butanol extract of celery (Apium graveolens) seed in streptozotocin-induced diabetic male rats." 4: 24-29.
7. Alhowiriny, T., A. Alsheikh, S. Alqasoumi, M. Al-Yahya, K. ElTahir and S. Rafatullah (2010). "Gastric antiulcer, antisecretory and cytoprotective properties of celery (Apium Graveolens) in rats." Pharmaceutical biology 48: 786-793.
8. Ali, R. A. (2003). "Management of diabetic neuropathy." The Malaysian journal of medical sciences : MJMS 10(2): 27-30.
9. American Diabetes, A. (2009). "Diagnosis and classification of diabetes mellitus." Diabetes care 32 Suppl 1(Suppl 1): S62-S67.
10. Amir-Aslani, A. and V. Mangematin (2010). "The future of drug discovery and development: Shifting emphasis towards personalized medicine." Technological Forecasting and Social Change 77(2): 203-217.

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