



ORIGINAL RESEARCH PAPER

Medical Science

ADVERSE REACTIONS BY RAW MATERIALS AND ITS ANTIDOTE FROM SIDDHA SYSTEM OF MEDICINE

KEY WORDS: Adverse Reactions, Antidote, Siddha system of Medicine

Dr. K. Naga Palani Saraswathi

PG Scholar, Department of Nanju Maruthuvam (Siddha Toxicology), Govt. Siddha Medical College, Tirunelveli, The Tamil Nadu Dr. M. G. R. Medical University, Chennai.

Prof. Dr. M. Thiruthani*

MD(s) Professor & Head of the Department, Department of Nanju Maruthuvam (Siddha Toxicology), Government Siddha Medical College, Tirunelveli.
*Corresponding Author

ABSTRACT

Typically, interactions between drugs come to mind (drug-drug interaction). However, interactions may also exist between drugs and foods (drug-food interactions), as well as drugs and herbs (drug-herb interactions). These may occur out of accidental misuse or due to lack of knowledge about the active ingredients involved in the relevant substances. Interactions between food and drugs may inadvertently reduce or increase the drug effect. Research Design: collect the literature evidences from selected Tamil Siddha books. Grouping the collected data then presentation of the data with discussion and conclusion. 50 adverse reactions of food to food & food to drug interactions managed by 65 antidote plants and 22 animal & minerals products. Fabaceae, Zingiberaceae, Cucurbitaceae, Apiaceae, Asclepiadiaceae & Rutaceae plant families which habits as; herbs and Trees were mostly occupied to management of adverse reactions. Leaves and seeds were mostly used parts as preparation of siddha medicine to manage adverse reactions. And this research strongly recommended to do the Clinical trials on these aspect of adverse reactions in future.

INTRODUCTION

Diet and lifestyle can sometimes have a significant impact on drugs. A drug interaction is a situation in which a substance affects the activity of a drug, i.e. the effects are increased or decreased, or they produce a new effect that neither produces on its own. Typically, interactions between drugs come to mind (drug-drug interaction). However, interactions may also exist between drugs and foods (drug-food interactions), as well as drugs and herbs (drug-herb interactions). These may occur out of accidental misuse or due to lack of knowledge about the active ingredients involved in the relevant substances. Interactions between food and drugs may inadvertently reduce or increase the drug effect.[2] Some commonly used herbs, fruits as well as alcohol may cause failure of the therapy up a point of to serious alterations of the patient's health. The majority of clinically relevant food-drug interactions are caused by food-induced changes in the bioavailability of the drug.[2]

Major side-effects of some diet (food) on drugs include alteration in absorption by fatty, high protein and fiber diets.[4] Bioavailability is an important pharmacokinetic parameter which is correlated with the clinical effect of most drugs. However, in order to evaluate the clinical relevance of a food-drug interaction the impact of food intake on the clinical effect of the drug has to be quantified as well. The most important interactions are those associated with a high risk of treatment failure arising from a significantly reduced bioavailability in the fed state. Such interactions are frequently caused by chelation with components in food. In addition, the physiological response to food intake, in particular, gastric acid secretion, may reduce or increase the bioavailability of certain drugs.[5,6]

Drug interactions can alter the pharmacokinetics and/or pharmacodynamics of a drug. The pharmacodynamic interaction may be additive, synergistic, or antagonistic effects of a drug. Drug interactions (DIs) represent an important and widely under recognized source of medication errors.[7] The gastrointestinal absorption of drugs may be affected by the concurrent use of other agents that, I have a large surface area upon which the drug can be absorbed,[4] bind or chelate,[5] alter gastric pH,[6] alter gastrointestinal motility, or affect transport proteins such as P-glycoprotein. A

reduction only in absorption rate of a drug is seldom clinically important, whereas a reduction in the extent of absorption will be clinically important if it results in sub therapeutic serum levels.[7]

Factors such as nonspecific binding, atypical kinetics, poor effector solubility, and varying ratios of accessory proteins may alter the kinetic behavior of an enzyme and subsequently confound the extrapolation of in vitro data to the human situation.[8] Coenzyme Q-10 (CoQ10) is very widely consumed by humans as a food supplement because of its recognition by the public as an important nutrient in supporting human health. It interferes with intestinal efflux transporter P-glycoprotein (P-gp) and as result food-drug interactions arise.[9]

The interaction of natural products and drugs is a common hidden problem encountered in clinical practice. The interactions between natural products and drugs are based on the same pharmacokinetic and pharmacodynamic principles as drug-drug interactions. Several fruits and berries have recently been shown to contain agents that affect drug-metabolizing enzymes.[10] Grapefruit is the most well-known example, but also sevillean orange, pomelo and star fruit contain agents that inhibit cytochrome P450 3A4 (CYP3A4), which is the most important enzyme in drug metabolism.[11]

The study of drug-drug, food-drug, and herb-drug interactions and of genetic factors affecting pharmacokinetics and pharmacodynamics is expected to improve drug safety and will enable individualized drug therapy. Drugs can show their efficacy only if administered in appropriate quantity with appropriate combination of drugs and foods and at appropriate time.[2]

In contrast to the easy access to information on drug-drug interactions, the information about food-drug interaction is not always available conveniently. It is a difficult and complex problem to accurately determine the effects of food and nutrients on a particular drug.[2]

Electronic search of literatures was conducted over a period of two months and all original research and review articles

were included in this study. No literature was older than 20 years. The drugs were selected and reviewed on the basis of their general utilization pattern and realizing the need for reporting their interaction with different dietary supplements for better therapeutic use of these drugs within the recommended dose regimen.

This article aims to help the healthcare professionals specially physicians and pharmacists and patients to become more knowledgeable about drug and food interactions and its management with herbo-mineral origin siddha medicines.

MATERIALS AND METHODS

Research Type: Literature Review

Research Design: collect the literature evidences from selected Tamil Siddha books. Grouping the collected data then presentation of the data with discussion and conclusion. Source of Literature: Siddha Toxicology, written by Dr. K. S. Murugesu Mudaliar, Revised by Dr. Pon. Gurusironmani and translated by; P. Jeyaraj, Published by. Department of Indian Medicine and Homoeopathy, Chennai 600 106. [1]

RESULT

Table1: Antidote plants for Adverse reaction produced plant list[1]

s.no	Adverse reactions produce plant name (in Tamil)	Antidote plant name (in Tamil)
1.	Ulunthu	Kollukai velai
1.		Milagu
1.		Seeragam
1.		Thean
2.	Kadalai, Thuvarai, Mochai	Chemman
3.	Nei	Pasum paal
4.	Nei + Thean	Kaari + neer
5.	Verkadalai	Karumbu vellam
6.	Thenkaai	Karumbu vellam
		Paatcharisi
7.	Koolimuttai	Mullangi kilangu
8.	Vaazhai pazham	Pugaiilai
9.	Pala pazham	Nei
1.		Thean
10.	Paladai	Pulitha moor
11.	Paaledu	Thean
12.	Elavam pisin	Sivanarvembu +neer
13.	Kuntrimani	Vengaram
1.		Vidathari
14.	Oonan kizhangu	Vellai sangam pazhacharu
15.	Navar kottai	Kollu
16.	Kodarkizhangu	Avuri + neer
17.	Milagai	Koththa malli+nei
18.	Sivanar kizhangu	Chukku
		Vellari
		Naval
19.	Magilam	Uththamani +chunnambu
20.	Sooru	Seeragam
		Kollukai velai +veneer
21.	Maruthontri + ennai	Thantrikai
22.	Nungu	Perungayam
23.	Pulitha thayir sooru	Kadugu
24.	Kodikalli paal	Koovai
		Pasu saani paal

		Vellai man + neer
25.	Nallennai +Sooru	Kaadi
26.	Vetrilaichaaru + nallennai	Thenkaipaal
27.	Nelver ennai	Surai
		Elumichai
28.	Nelver sarkkarai	Erukku
29.	Nelver	Peipirkku
		Vilamicham
30.	Kothumbai	Milagai
31.	Ennai	Oosarpattai
32.	Erukku	Sarkkarai +ellu
		Paruthi + kaadi
		Manjal +sitraamanakku
		Nallennai
		Maavilingam
33.	Sathurakallipaal	Aavarai
34.	Thillai paal	Koovai
		Sitraamanakku
		Erumai saani paal
		Erumai nei
35.	Nervalam	Vasambu +puli
		Thean + seeragam
		Neichitti
		keerai+Murungai+
		pannirchedi+ seeragam
36.	Chithiramoolam ver	Pasu nei
		Nallennai +ulunthu
		Peipirukku +
		korakizhangu
37.	Senkottai	Senkkal
		Nallennai
		Korakizhangu
		+santhanam+ ellu + elarisi
		+thean
		Puli + neer+ ilaneer+
		theankkai
38.	Manjal alari + ennai	Kadukkai
		Kappai kizhangu
		Thurusu + veneer
39.	Umaththai	Thamarai + pulitha
		thaneer
1.		Neeli + pulitha thaneer+
		alinjil +elumichai
40.	Eetti kottai	Naaval
		Thamarai
		Oonan ilai
		Kadukkai
		Avuri
	Neer	Thean + neer
		Vetrilai
		Venthaiyam +milagu
		+vennai
41.	Abini	Elaikalli +korakizhangu
		+vasambu +chukku
42.	Kanja	Chukku
1.		Elummichai
1.		Vaalai

43.	Naabi	Kasini +pasumpaala or nei
		Pantri malam + pasu nei
		Kaddukkai
		Puthirasogi +pasunei
		Vengaaram + pasunei
		Milagu +pasunei
		Patchai meenin oon +pasu vennai
		Mayil thuththam +mulaipaala
44.	Pugailai	Agathi
		Kurinchanilai + vellulli + narseeragam
45.	Eraththampolam	Perrathai
46.	Purumarunthu	Milagu
47.	Uloga parpa senthura maathirai	Ayachenthuram parpam
		Ayakalantha maathirai
48.	Kudineer	Uththamani
49.	Unavu	Kulirintha neer
50.	Neer	Thean + neer

19	Perungayam	Ferula asafoetida	Apiaceae	Shrub	Resin
20	Kadugu	Brassica juncea	Brassicaceae	Herb	Seed
21	Koovai	Coccinia grandis	Cucurbitaceae	Climber	Leaf
22	Thenkaipaal	Coccoloba nucifera	Arecaceae	Tree	Coconut milk
23	Surai	Lagenaria siceraria	Cucurbitaceae	Climber	Unripe fruit
24	Elumichai	Citrus medica	Rutaceae	Tree	Fruit
25	Erukku	Calotropis gigantea	Asclepiadaceae	Shrub	Leaf, latex
26	Peipirkku	Luffa acutangula	Cucurbitaceae	Creeper	Seed
27	Vilamichai	Plectranthus vettiveroides	Lamiaceae	Grass	Root
28	Oosarpattai			Climber	Bark
29	Ellu	Sesamum indicum	Pedaliaceae	Herb	seed, seed oil
30	Paruthi	Gossypium hirsutum	Malvaceae	SubShrub	Leaf
31	Manjal	Curcuma longa	Zingiberaceae	Herb	Rhizome
32	sitraamana kku	Ricinus communis	Euphorbiaceae	Shrub	Seed
33	Maavilingam	Crataeva magna	Capparidaceae	Tree	Bark
34	Aavarai	Cassia auriculata	Caesalpiniaceae	Shrub	Leaves
35	Vasambu	Acorus calamus	Acoraceae	Herb	Root
36	Puli	Tamarindus indica	Caesalpiniaceae	Tree	Leaf
37	Neichitti keerai	Vernonia cinerea less	Asteraceae	Herb	Leaves
38	Murungai	Moringa oleifera	Moringaceae	Tree	Leaves
39	pannirchedi	Guettarda speciosa	Rubiaceae	Shrub	leaves
40	ulunthu	Vigna mungo	Fabaceae	Herb	Seed
41	koraikizhangu	Cyperus rotundus	Araceae	Creeper	Root tuber
42	santhanam	Santalum album	Santalaceae	Tree	Wood
43	elarisi	Elettaria cardamomum	Zingiberaceae	Shrub	Seed
44	Puli	Tamarindus indica	Caesalpiniaceae	Tree	Leaf
45	ilaneer	Coccoloba nucifera	Arecaceae	Tree	Tender coconut
46	Kadukkai	Terminalia chebula	Combretaceae	Tree	Fruit
47	Kalappai kizhangu	Gloriosa superba	Liliaceae	Climber	Root tuber
48	Thamarai	Nelumbo nucifera	Nymphaeaceae	Water plant	Rhizome
49	alinjil	Alangium salvifolium	Comaceae	Tree	Root bark
50	elumichai	Citrus medica	Rutaceae	Shrub	Fruit
51	Oonan ilai	Ipomoea racemosa	Convolvulaceae	Climber	leaves
52	Vettilai	Piper bettle	Piperaceae	Climber	Leaf
53	Venthaiyam	Trigonella foenum	Fabaceae	Herb	Fruit
54	Elaikalli	Euphorbia nerifolia	Euphorbiaceae	Tree	Root

Table 2: Antidote plants' list with botanical aspect and used parts

	Antidote plant name (in Tamil)	Botanical name	Family	Habit	Part used
1	Kollukai velai	Tephrosia purpurea	Fabaceae	Herb	Whole plant
2	Milagu	Piper nigrum	Piperaceae	Climber	Seed
3	Seeragam	Cuminum cyminum	Apiaceae	Herb	Dry fruit
4	Karumbu vellam	Saccharum officinarum	Poaceae	Shrub	Sugar
5	Paatcharisi	Oryza sativa	Poaceae	Herb	Raw rice
6	Mullangi kilangu	Raphanus sativus	Brassicaceae	Herb	Rhizome
7	Pugailai	Nicotiana tabacum	Solanaceae	Herb	Leaf
8	Sivanarvembu	Indigofera aspalathoides	Fabaceae	Herb	Root
9	Vidathari	Dichrostachys cinerea	Fabaceae	Shrub	Leaf
10	Vellai sangam pazhacharu	Clerodendrum inermis	Verbenaceae	Shrub	Fruit
11	Kollu	Dolichos biflorus	Fabaceae	Herb	Seed
12	Avuri	Indigofera tinctoria	Fabaceae	Herb	Root bark
13	Koththamalli	Coriandrum sativum	Apiaceae	Herb	Dry fruit
14	Chukku	Zingiber officinale	Zingiberaceae	Herb	Rhizome
15	Vellari	Cucumis sativus	Cucurbitaceae	Creeper	Seed
16	Naval	Syzygium cumini	Myrtaceae	Tree	Seed
17	Uththamani	Pergularia daemia	Asclepiadaceae	Climber	Leaf, root, stem
18	Thantrikai	Terminalia bellirica	Combretaceae	Tree	Dried fruit

55	Vaalai	Musa serpentina	Musaceae	Tree	Bark
56	Kasini	Cichorium intubus	Asteraceae	Herb	Leave
57	Puthirasogi	Putran-jiva roxburghii		Tree	Seed
58	Sirukeerai	Amaranthus tricolor	Amarantha ceae	Herb	Leaves
59	omam	Carum copticum	Umbilifera ceae	Herb	seed
60	vilampattai	Limonia acidissima	Rutaceae	Tree	Bark
61	Agathi	Sesbania grandiflora	Fabaceae	Shrub	Leaves
62	Kurinchanil ai	Dregia volvulus	Convolvula ceae	Climber	Leave
63	vellulli	Allium sativum	Liliaceae	Herb	Bulb
64	Perrathai	Alpinia galangal	Zingiberac eae	Herb	Rhizome
65	Uththamani	Pergularia daemia	Asclepiada ceae	Climber	Root

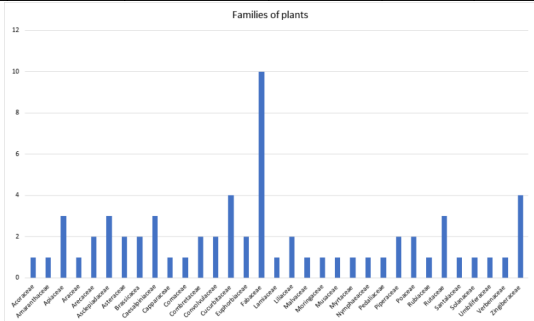


Chart 1: Antidote plants' family list

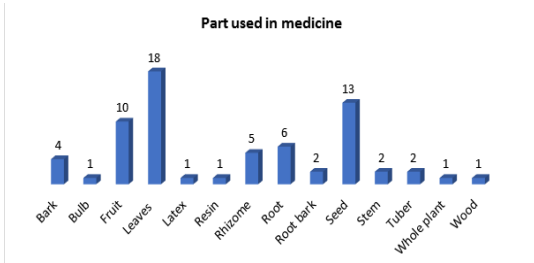


Chart 2: part used of anti-dote plants

Table 4: habits of Anti-dote plants

Habit	No. of plants
Climber	10
Creeper	3
Grass	1
Herb	22
Shrub	12
Tree	16
Water plant	1

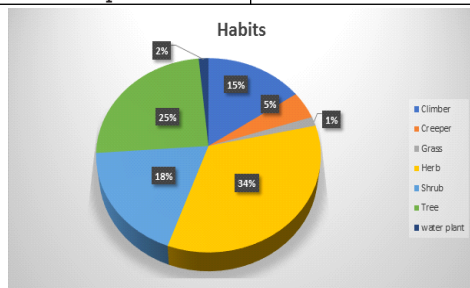


Chart 3: percentage of habits of antidote plants

Table 3: list of Antidote animal & mineral products for Adverse reaction produced

	Antidote Animal & mineral product (in Tamil)	English name
1	Thean	Honey
2	Chemman	Red sand
3	Pasum paal	Cow's milk
4	Kari + neer	Charcoal + water
5	Nei	Ghee
6	Pulitha moor	Butter milk
7	Vengaram	Borax
8	Chunnambu	lime stone
9	Pasu saani paal	Cow's dung
10	Vellai man + neer	White sand + water
11	Erumai saani paal	Buffalo dung
12	Erumai nei	Buffalo ghee
13	Pasu nei	Cow's ghee
14	Senkkal	Stone of red sand
15	Pantri malam + pasu nei	Pig dung + cow's ghee
16	Vengaaram + pasunei	Borax + cow's ghee
17	Patchai meenin oon + pasu vennai	Flesh of fish + cow's butter
18	Mayil thuththam + mullaipaal	Copper sulphate + mother's milk
19	Aya chenthuram parpam	higher order medicine
20	Aya kalantha maathirai	higher order medicine
21	Kulirinta neer	cool water
22	Thean + neer	honey and water

DISCUSSION & CONCLUSION

According to result; Siddha toxicology text explained 50 adverse reactions of food to food & food to drug interaction respectively. These adverse reactions managed by specific antidote also prescribed in this siddha authenticate literature clearly. Hence, 65 antidote plants and 22 animal & minerals products were list out as antidote to adverse reactions. Among 65 plant antidotes; 33 families were occupied to widespread to management which was Fabaceae is mostly used as 10 plants out of 65 plants, 04 plants belong from Zingiberaceae, Cucurbitaceaea and 03 plants belong from Apiaceaea, Asclepiadiaceae & Rutaceae were notifiable.

In the result of parts used for management; 14 types of parts were list out. Among these, 18 no. of leaves, 13- seeds, 10- fruits, 06- roots and 05- rhizomes were notifiable.

Habits of the anti-dote plants were noticed as; total 07 habits which were herbs- 22 (34%), Trees- 16 (25%), Shrubs - 12 (18%), Climbers - 10 (15%) and others less than 15%.

Finally concluded as; 50 adverse reactions of food to food & food to drug interactions managed by 65 antidote plants and 22 animal & minerals products. Fabaceae, Zingibercaea, Cucurbitaceaea, Apiaceaea, Asclepiadiaceae & Rutaceae plant families which habits as; herbs and Trees were mostly occupied to management of adverse reactions. Leaves and seeds were mostly used parts as preparation of siddha medicine to manage adverse reactions. Therefore, in this research revealed that, siddha medicine had effective management for adverse reaction of food to food reaction and food to drug reaction from ancient time with natural product basis siddha medicines respectively. And this research strongly recommended to do the Clinical trials on these aspect of adverse reactions in future because these crises will be facing soon by the modern health world.

ACKNOWLEDGEMENT: I sincere thank to my Professor and Head of the Department Dr. M. Thiruthani MD(s), PGDYN. for his encouragement to do researches. And I express my thanks

to all staff of Post Graduate Department of Siddha Toxicology, Govt. Siddha Medical College, Tirunelveli affiliation in The Tamil Nadu Dr. M. G. R. Medical University, Chennai.

CONFLICT OF INTEREST: No any conflict of interest in this article.

REFERENCES

[1] Murugesha Mudaliar K. S., Revised by Dr. Pon. Gurusironmani and translated by; P. Jeyaraj, Siddha Toxicology, Published by. Department of Indian medicine and homoeopathy, Chennai 600 106., edition, 2013, pages; 128-141.

[2] Bushra R, Aslam N, Khan AY. Food-drug interactions. *Oman Med J*. 2011;26(2):77-83. doi:10.5001/omj.2011.21

[3] Frankel EH. (2003). Basic Concepts. In: *Hand book of food-drug Interactions*, McCabe BJ, Frankel EH., Wolfe JJ (Eds.) pp. 2, CRC Press, Boca Raton, 2003.

[4] Ayo JA, Agu H, Madaki I. Food and drug interactions: its side effects. *Nutr Food Sci* 2005;35(4):243-252

[5] Schmidt LE, Dalhoff K. Food-drug interactions. *Drugs* 2002;62(10):1481-1502.

[6] Nekvindová J, Anzenbacher P. Interactions of food and dietary supplements with drug metabolising cytochrome P450 enzymes. *Ceska Slov Farm* 2007 Jul;56(4):165-173.

[7] Hansten PD. (2004) Appendix II: important interactions and their mechanisms, In: Katzung BG. (2004). editor, 9th edn, (2004) *Basic and clinical Pharmacology*, McGraw hill, Boston pp 1110.

[8] Itagaki, S., Ochiai, A., Kobayashi, M., Sugawara, M., Hirano, T., Iseki, K. (2008). Interaction of Coenzyme Q10 with the Intestinal Drug Transporter P-Glycoprotein. *J Agric Food Chem*. 27;56(16):6923-7.

[9] Joshi R, Medhi B. Natural product and drugs interactions, its clinical implication in drug therapy management. *Saudi Med J* 2008 Mar;29(3):333-339.

[10] Molden E, Spigset O. Fruit and berries—interactions with drugs. *Tidsskr Nor Laegeforen* 2007 Dec;127(24):3218-3220. Kirby BJ, Unadkat JD. Grapefruit juice, a glass full of drug interactions? *Clin Pharmacol Ther* 2007 May;81(5):631-633.