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EFFECT OF *KOROSANAI MATHIRAI* ON PEDIATRIC CARE- A SYSTEMATIC REVIEW

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ABSTRACT

At present, there are *Ayurveda, Siddha, Unani* and *DeshiyaChikitsa* in Sri Lanka. According to *Siddha*, 108 diseases are said to occur during childhood. *Agathyar* classified the pediatric diseases into many subtypes based on the clinical symptoms/signs. The *KorosanaiMathai (K.M)* is a mixture of *Korosanai*, some herbal material and minerals. *Ayurvedic* practitioners in Jaffna peninsula of Northern Sri Lanka have been prescribing*K.M*for pediatrics for their respiratory disorders, fever, cold, gastro intestinal problems and skin diseases with suitable *Anupanam*. The objective of the study to list out the ingredients of the *K.M* in various Siddha text books and to describe the way of curing the pediatric diseases by their pharmacological properties. A comprehensive systematic review was conducted in the following thesis, research articles and the journals were referred through globally accepted websites. To obtain additional data, a manual search was performed using the reputed siddha literatures. *K.M* formulations were found from various *Siddha* text books. Most of the formulations were consisted of *Capra aegagrus, Saussurea costus, Parietaria judaica,* Nigella sativa, *Quercus infectoria and Piper longum***.** *K.M* were mostly using in gastrointestinal problems, respiratory disorders and skin disorders. The ingredients of *K.M*formulations had many pharmacological activities. According to our findings pharmacological properties of *K.M* is more effective on pediatric disease management.

KEY WORDS: *Korosanai, Mathirai, Agasthiyar*

1. INTRODUCTION

1.1 Introduction of indigenous medicine

Traditional medicine has been practiced in Sri Lanka for 3,000 years. At present, there are four systems of traditional medical systems in Sri Lanka viz. *Ayurveda, Siddha, Unani* and *DeshiyaChikitsa* (Sri Lankan traditional treatment) (Kamal Perera ,2017). The main aim of *Siddhars* is "to prevent disease rather than cure". The preventive principles are explained elaborative in the text *"Theraiyar Pinianuga vithiozhukkam"* which describes the daily and seasonal regimens to be followed by the people to prevent diseases (Subramanian, *et al* 1984). With strong basic principles and cultural background, *Siddha* system of medicine is providing health care solutions to a number of health issues of the modern era. Though it is a system of medicine, Siddha system is guiding us to lead to a perfect living in this world, starting from conception to death. Not only that, the system takes care even before the conception itself (Meenakshi *et al* 2017)

1.2 Children's health

Children's health is or pediatrics, focuses on the well-being of children from conception through adolescence. It is vitally concerned with all aspects of children's growth and development and with the unique opportunity that each child has to achieve their full potential as a healthy adult. Children's health care was once a part of general medicine. It emerged in the 19th and early 20th century as a medical specialty because of the gradual awareness that the health problems of children are different from those of grown-ups. It was also recognized that a child's response to illness, medications, and the environment depends upon the age of the child (David *et al*, 2011*)*

1.3 Pediatric medicine in Siddha

According to *siddha* system of medicine total number of diseases is 4448 in number. Of these, 108 diseases are said to occur during childhood. *Agathyar*, who is considered as the father of *Siddha* medicine classified the pediatric disease into many subtypes based on the clinical symptoms/signs. There are *Maantham* (GIT Problems), *Kanam*(Complicated Lower respiratory Infections), *Kirumi* (Worms' infestation), *Paandu* (Anemia), *Sobai* (Edema), *Kaamaalai* (Jaundice), *Lasunathaabitham* (Tonsillitis), *Suram* (Fever), *Erumal* (Cough), *Baalavaatham* (Poliomyelitis, Cerebral palsy), *Thasaivaatham* (Myopathy), *Moolaivalarchikuraivu* (Mental retardation), *Venpadai* (Leucoderma), *Sirangu* (Scabies), *Seethakkazhichal* (Dysentery), *Puzhuvettu* (Alopecia), *Akkaram* (Stomatitis),

Kalaanjagapadai (Psoriasis), *Marul* (Wart), *Karappaan* (Eczema), *Thavalaichori* (Phrynoderma/toad skin disease), *Tholvaratchinoi* (Dryness of the skin), *VithaiNoigal* (Diseases of the testis), *Kabasuram* (Fever with respiratory Infections), *Peenisam* (Sinusitis), *Eraippu irumal* (Bronchial asthma) and *Padarthaamarai* (Ringworm). *Siddhars* have enumerated various effective internal and external remedies for the above said conditions. (Subramanian *et al* 1984, MeenakshiSundaram*et al* 2017),The Text book dealing with Pediatrics in *Siddha* system is called as *"Balavagadam". "Balavagadam"* is the branch of medicine dealing with the diseases of the children and their management & treatment through Siddha System of Medicine or Care of infants and children through Siddha way (Gurusironmani,1992).

1.4 Introduction of Korosanaimathirai.

The *KorosanaiMaathrai* is a mixture of *Korosanai*(Cow bezoar), some herbal material and minerals. Ayurvedic doctors in Jaffna peninsula of Northern Sri Lanka have been prescribing *korosanaimaththirai* for babies for their good health such as mostly fever, cold, Gastro intestinal problems and skin diseases with suitable *anupanam (Vehicle).* It has been believed by the Ayurvedic practitioners that the above mixture causes a strong effect on immune system. (MeenakshiSundaram*et al* 2017). The formulations are using plant raw drugs and contain very less ingredients of Mineral drugs. Most of these medicines are administered in breast milk as it contains necessary immunity factors for the child. The formulations are mostly in the form of decoction and tablets as these forms are easily absorbed in the circulation. (SubramaniParasuraman, 2014).

The review process is adopted to collect various *Korosanai maththirai* formulations for the indication pediatric diseases mentioned in published *Siddha* texts. The data was summarized and list of majority herbs used in the formulations are identified. The pharmacological activity of each herb, identified by standard scientific procedures and documented in open access scientific journals is sorted out by searching in internet with their botanical name as keyword. Inclusion and exclusion criteria only the name mentioned as *Korosanai maththirai* are included. Other formulations such as *Thakkalisatrukorosanaimaththirai, KaakanavanKorosanaimaththirai, Periyakorosanaimaththirai,*are not included in the review.

2.DRUG REVIEW

Preparation methods of *korosanaimaththirai*mentioned in various texts:

1*Kalanju*- 5.1g, 1*varagan* - 4.2g

Table 1: According to text of *Siddamaruththuvasudar*, Dr.M. Sowrirasan

Botanical name	**Tamil name**	**Parts use**	**Ratio**
Quercusinfectoria	*Maasi kai*	Gall	10g
Piper longum	*Thippali*	Dry fruit	10g
Capra aegagrus / Bezoar	*Korosanai*	Bile Secretion	10g
Saussureacostus	*Koddam*	Root	10g
Nigella sativa	*Karumseerakam*	Dry fruit	10g
Parietariajudaica	*Akkirakaram;*	Root	10g

Preparation procedure:

Grind all the ingredients

Paste with breast milk

Make a pill as a size of *Abrusprecatorius (Kunrimaniedai) (0.27g)* and dry on shadow

Dosage: P1 Morning and Night

Indication: Indigestion, Phlegm, Hoarseness of voice

***Pathiyam*(Diet and regiment):** Mother should avoid *Tamarindusindicus*(*Palapuli*)in her meals

Table 2: According to text of Pararasasegaram *part 2*, Palaroganithanam

Botanical name	**Tamil name**	**Parts use**	**Ratio**
Quercusinfectoria	*Maasi kai*	Gall	5.1g
Piper longum	*Thippali*	Dry fruit	5.1g
Capra aegagrus / Bezoar	*Korosanai*	Bile Secretion	5.1g
Saussureacostus	*Koddam*	Root	5.1g
Nigella sativa	*Karumseerakam*	Dryfruit	5.1g
Parietariajudaica	*Akkirakaram*	Root	5.1g
cuminumcyminum	*Natseerakam*	Dryfruit	5.1g
Sagasthiravaydi	*Saththirapethi*	Mineral	5.1g

SyzygiumAromaticum	*Karambu*	Buds	5.1g
Croton tiglium	*Purified nervalam*	Seed	5.1g

Preparation procedure:

Grind all the ingredients

Paste with *Clitoriaternatea(Kaakanavan) leave* juice

Make a pill as a size of green gramand dry on shadow

Dosage: P1 with breast milk and *Plectranthusamboinicus (Katpooravalli)* leave juice

Indication: Skin rash or eczema

Table 3: According to text of Pararasasegaram *part 2*, Palaroganithanam

Botanical name	**Tamil name**	**Parts use**	**Ratio**
Quercusinfectoria	*Maasi kai*	Gall	5.1g
Capra aegagrus / Bezoar	*Korosanai*	Bile Secretion	5.1g
Myristicafragrans	*Sathikkai*	Dried fruit	5.1g
Zing sulphate / Zincum	*Paatkerudapachchai*	Mineral	5.1g
Asbestos	*Kalnaar*	Mineral	5.1g
Sagasthiravaydi	*Kanithapethi*	Mineral	5.1g

Preparation procedure:

Grind all the ingredients

Paste with *coconut water and peramaddi*juice

Make a pill as a size of cotton seed *and* dry on shadow

Dosage and Indication:

P1 with unripe fruit of cotton for- Diarrhea

P1 with warm water for fever and P1 with *Terminalia chebulla (Kadukai)* decoction for Constipation

Table 4: According to text of Siththa*vaithiyathiraddu*

Botanical name	**Tamil name**	**Parts use**	**Ratio**
Capra aegagrus / Bezoar	*Korosanai*	Bile Secretion	*15.75g*

Crocus sativus	*Kungumapo*	Stigmas and styles	*15.75g*
Boro camphor/ Borneol	*Pachchaikatpooram;*	Mineral	*15.75g*
Myristicafragrans	*Sathikkai*	Dried fruit	*15.75g*
Cinnamomumzeylanicum	*Ilavangam*	Bark	*15.75g*
Elettariacardamomum	*Elam*	Dried fruit	*15.75g*
Saussureacostus	*Koddam*	Root	*15.75g*
Parietaria Judaica	*Akkaraakaram;*	Root	*15.75g*
Camphoraofficinarum	*Katpooram*	Plant Secretion	*15.75g*
Hydrargyrum	*Rasa senthuram*	Mineral	*15.75g*
Mica	*Appirakapatpam*	Mineral	*15.75g*

Preparation procedure:

Grind all the ingredients

Paste with decoction of sandal wood &*Magnolia champaca* flower (*Senpaka poo)* for 4 *saamam (16 hours)*

Then paste with *Crocus sativus(Kungumapoo)decoction* for 2 *saamam (8 hours)*

Make a pill as a size of *Abrusprecatorious*(*Kunrimaniedai*) (0.27g) seed and dry on shadow.

Dosage: P1 with breast milk

Indication: Faint, gas trouble,phlegm, cold and fever, coma, Headache.

Table 5: According to text of Balavakadam,Dr. Pon.Gurusironmani

Botanical name	**Tamil name**	**Parts use**	**Ratio**
Quercusinfectoria	*Masikkai*	Gall	*Equal part*
Piper longum	*Thippali*	Dried fruit	*Equal part*
Capra aegagrus / Bezoar	*Korosanai*	Bile Secretion	*Equal part*
Saussureacostus	*Sathikoddam*	Root	*Equal part*
Nigella sativa	*Karumseerakam*	Dried fruit	*Equal part*
Parietariajudaica	*Akkarakaram*	Root	*Equal part*

Preparation procedure:

Grind all the ingredients

Paste with breast milk

Make a pill as a size of *Pepper* seed and dry on shadow.

Dosage: P1 with breast milk

Indication: Diarrhea and indigestion

Table 6: According to text of *Kaimurai packet vaithiyam*, P.S.Thulasingamuthaliyar

Botanical name	**Tamil name**	**Parts use**	**Ratio**
Piper nigrum	*Milaku*	Dried fruit	*6.3g*
Cinnamomumzeylanicum	*Ilavankam*	Bark	*6.3g*
Myristicafragrans	*JAthikkai*	Dried fruit	*6.3g*
Trachyspermumammi	*Omam*	Dried fruit	*4.2g*
Myristicafragrans	*Jathipaththiri*	Dried leaf	*4.2g*
Plumbagozeylanica	*Siththiramoolam*	Root	*4.2g*
Piper longum	*Thippali*	Dried fruit	*6.3g*
Nigella sativa	*Karumseerakam*	Dryfruit	*4.2g*
Saussureacostus	*Koddam*	Root	*4.2g*
Capra aegagrus / Bezoar	*Korosanai*	Bile Secretion	*8.4g*
Syzygiumcumini	*Naavalthulir*	Tender leaf	*4.2g*
Mangiferaindica	*Maathulir*	Tender leaf	*4.2g*
Azadirachtaindica	*Vemukolunthu*	Tender leaf	*4.2g*
Hydrargyri sub chloridum	*Pooram*	Mineral	*4.2g*

Preparation procedure:

Grind all the ingredients

Paste with *Clitoriaternatea leave(Kakanavan)*juice

Make a pill as a size of green gramand dry on shadow

Dosage: P1 with breast milk and *Plectranthusamboinicus(Katpooravalli)* leave juice

Indication: Skin rash or eczema

Table 7: According to text of Patharthakunavilakkam, Thaathugeevavarkam, VaitiyavithvanmaniS.Kannusamipillai

Botanical name	**Tamil name**	**Parts use**	**Ratio**

Capra aegagrus / Bezoar	*Korosanai*	Bile Secretion	*2.1g*
Crocus sativus	*Kunguma poo*	Stigmas and styles	*2.1g*
Boro camphor/ Borneol	*Pachchaikatpooram*	Mineral	*2.1g*
Canariumstrictum	*Sambiranipathankam;*	Resin	*2.1g*
Glycyrrhiza glabra	*Athimaduram*	Root	5.1g
Zingiberofficinale	*Sukku*	Rhizomes	5.1g
Elettariacardamomum	*Elam*	Dried fruit	5.1g
Saussureacostus	*Koddam*	Root	5.1g
Parietariajudaica	*Akkarakaram*	Root	5.1g
Artemifianilagirica	*Masipaththiri*	Dried leaf	Needful Decoction
Santalum album	*Santhanam*	Heart wood	Needful Decoction
Chrysopogonzizanioides	*Vettiver*	Root	Needful Decoction

Preparation procedure:

Grind all the ingredients

Paste with separate decoctions*of Artemisia nilagirica (Masipathtiri),Santalum album (Vensanthanam) and Chrysopogonzizanioides*for 2 hours.

Make a pill as a size of green gramand dry on shadow

Dosage: P1 with breast milk, Honey and zinger juice

Indication: *Thosam, Suram,Sanni, Thondaikaddu*

2.1 Raw ingredients were mostly using in pediatric disorders

Six(6) K.M formulations were founded from various siddha text books. Most of the Korosanaimathirai formulations were consisted *Capra aegagrus, Saussureacostus, Parietaria judaica,* Nigella sativa, *Quercus infectoria, Piper longum* which have been widely used in the treatment of pediatric diseases.

2.1.1Cow Bezoar(Korosanai)

Scientific name*: Capra aegagrus*

Parts use: Bile secretion.

Active component: Calcium phosphocholine, calcium phosphate, Bilirubin

Pharmacology:

Action on the nervous system

Oral cow bezoar in mice antagonized convulsions elicited by camphor, caffeine and picrotoxin. It was most potent against camphor, next against caffeine and picrotoxin. Two consecutive doses of artificial cow bezoar, intragastrically given two mice at 200mg/kgat one-hour interval, followed by intra peritoneal injection of pentylenetrazole, demonstrated a significant anticonvulsionaction (Zhejiang medical college et al,1972)

Anti-microbial action

In vitro studies showed that cow bezoar directly deactivated encephalitis B virus. Cow bile could markedly inhibit the growth of *Bordetella pertussis* (Scientific research compilation,1966-1971).

Anti –inflammatory, Anti allergic and Detoxicant actions

The increased vascular permeability elicited by intra peritoneal injection of acetic acid in mice could be inhibited by cow bezoar. (Guangzhou No 3 Pharmaceutical factory,1971)). Granulation of implanted of formaldehyde-treated filter paper in mice was inhibited by cow bezoar.(Jiang MC et al,1978). Cow bezoar inhibited the migration of polymorphonuclear leucocytes(New chines medicine section,1972). Cow bezoar protected guinea pigs against histamine induced shock and mice against epinephrine-induced shock (Jiangsu college of new medicine,1975). These information suggests that cow bezoar and its constituents possess anti-inflammatory action.

Action on the respiratory system

Bezoar were containing antitussive, anti-histamine and expectorant action (Coronary disease prevention and treatment unit,1973).

Action on circulatory system

Calcium phosphate of cow bile stimulated the isolated toad heart, whereas bilirubin inhibited heart beat(Fuzhou Coordination Research group for the prevention and treatment of coronary disease,1973).Bezoar could also strengthen the cardiac contractility of isolated frog and guinea pig hearts(Coordinating research group for the prevention and treatment of coronary disease,1973) Bezoar dilated the blood vessels of the isolated rabbit ear and also

lowered the blood pressure of anesthetized rabbits. A significanthypertensive action was also demonstrated by bilirubin(Fuzhou Coordination Research group for the prevention and treatment of coronary disease,1973).

Action on the blood and hematopoietic system

In comparison with the control group, rabbits with acute hemorrhage treated with daily oral administration cow bezoar at 100mg/kg for 3 days increased reticulocytes and quickened normalization of erythrocytes count and hemoglobin and promote generation of erythrocytes (Coronary disease group, 1972).

Action on the digestive system.

The aqueous extract of cow bezoar given intragastrically to rats at 100mg (crude drug)/kg markedly increased bile secretion (7). In vitro experiment on pig common bile duct with intact Oddi's sphincter showed that bezoar had relaxant action and promoted the excretion of bile into the duodenum. Aqueous extract of bezoar had anti spasmodic action in acetychjodline-1induced spasms of the isolated mouse small intestine (Coronary disease treatment and prevention unit, -1973)

2.1.2Indian costuskut root (Koddam)

Botanical name*: Saussureacostus*

Parts use: Root

Active component: Costunolide, dehydrocostus lactone and cynaropicrin.

Pharmacology:

Different pharmacological experiments in a number of in vitro and in vivo models have convincingly demonstrated the ability of Saussureacostus to exhibit anti-inflammatory, anti-ulcer, anticancer and hepatoprotective activities, lending support to the rationale behind several of its traditional uses (Pandey *et al*,2007).

2.1.3 Spreading pellitory(Akkarakaram)

Botanical name*: Parietariajudaica*

Parts use: Root

Active component: Aqueous Extract-Flavonoids, Aqueous ethanol extract- Flavonoids and proteins, Ethanol extract-Terpinoid, Flavonoids, Protein, Chloroform- Flavonoids and proteins, Petroleum ether- Alkaloid and protein (EveraldoAttard et al ,2012)

Pharmacology:

Herb, decoction in bronchitis, pharyngitis, pulmonitis and cough; catarrh; kidney stones; hemorrhoids (Borg, 1927; Penza, 1969; CassarPullicino, 1947) his herb in phytotherapy is used to treat topical wounds and respiratory diseases. Some other properties including analgesic, anti-diarrheatic, hemorrhagic ulcer-treating, antimalarial, anti-inflammatory, antimicrobial and immunosuppressive effects have also been reported for this plant (Sarkhail et al,2006). Moreover, some sources have reported tonic, diarrhea and free radical-inhibitory effects (Hussin et al,2010).

2.1.4 Black cumin(Karumseerakam)

Botanical name*:* Nigella sativa

Parts use: Dry fruit

Active component : Extensive studies were done to identify the composition of the black cumin seed, the ingredients of *N. sativa* seed includes: fixed oil, proteins, alkaloid,saponin and essential oil (FatemehForouzanfar et al 2014)

Pharmacology: In recent years huge number of studies have been carried out, acclaimed medicinal properties emphasized on different pharmacological effects of *N. sativa* seeds such as antioxidant anti-tussive, gastro protective, anti-anxiety, anti-ulcer, anti-asthmatic , anti-cancer, anti-inflammatory, immunomodulatory and anti-tumor properties , hepatoprotective effect, also gastric ulcer healing, tumor growth suppression, men infertility improvement, cardiovascular disorders, memory improvement, stimulate milk production, protective effects on lipid peroxidation, antibacterial activity, anti-dermatophyte, antiviral activity against cytomegalovirus, have been reported for this medicinal plant(FatemehForouzanfar et al 2014).

2.1.5 Galloak (Masikkai)

Botanical name*:**Quercusinfectoria*

Parts use: Gall

Active component

The galls contain 50-70% of the tannin known as Gallo tannic acid. This is a complex mixture of phenolic acid glycosides varying greatly in composition. It is prepared by fermenting the galls and extracting with water-saturated ether (Evans, 2002). Tannin which is about 60-70% contains gallotannin, particularly hexa- andheptagalloyl- glucoses (Anonymous, 2000). The galls also contain gallic acid (about2-4%), ellagic acid, sitosterol, methyl betulate, methyloleanolate, starch and calcium oxalate. Nyctanthic, roburic and syringic acids have more recently been identified. Tannic acid is hydrolysable tannin yielding gallic acid and glucose and having the minimum complexity of pentadigalloylglucose. Solutions of tannic acid tend to decompose on keeping with formation of gallic acid, a substance which is also found in many commercial samples of tannic acid. It may be detected by the pink colour produced on the addition of a 5% solution of potassium cyanide (Evans, 2002). The galls also contain gum, sugar and essential oil (Anonymous, 2005). An Aleppo gall contains 50-60% of tannin (tannic acid). A Chinese gall contains 70% of tannic acid. Oak bark contains up to 16% tannic acid to which it owes its effects. Pure gallic acid is in the form of white or colorless feathery crystals of a beautiful silky luster; it is a commercial acid. However, it is pale-yellow in color, soluble in alcohol and also sparingly in ether. Its solution in water undergoes decomposition when exposed to air. Gallic acid is converted into meta-gallic acid when strongly heated (Nadkarni, 1954).Amentoflavonehexamethyl ether, iso-cryptomerine and beta-sito-sterol have also been isolated (Khare, 2004).

Pharmacology:

Anaesthetic

The local anaesthetic action of a sub fraction prepared by chloroform-methanolextraction of galls was found due to the complete blockade ofthe isolated frog sciatic nerve conduction. The data obtained indicates that it is apotent local anaesthetic. The action potential was completely abolished within 7minute when an isolated nerve was placed in a 4% solution of subfraction(Wasim Ahmad *et al*, 2016).

Analgesic

A dried acetone-treated methanol extract of gall dissolved in waterwas studied for its analgesic effect in an experimental model using the rat tail-flick test. The result showed analgesic effect in rats (Wasim Ahmad *et al*, 2016).

Anticancer

The study was carried out to determine the potential of galls as an ant proliferative agent towards the cervical cancer cells and ovarian cancercells. The toxicity in vitro was evaluated on non-malignant cell line. The resultssuggested that galls extracts have significant anticancer effect (Wasim Ahmad *et al*, 2016).

Antidiabetic

A dried acetone-treated methanol extract of galldissolved in water was studied for its hypoglycemic effect in an experimental model. The result revealed that it significantly reduced blood sugar level in rabbits (Wasim Ahmad *et al*, 2016).

Antihypertensive

Galls have been reported to cause a significant reduction in the blood pressure in rabbits (Wasim Ahmad *et al*, 2016).

Anti-inflammatory

A study was designed to evaluate anti-inflammatory effect of alcoholic extract of galls on various experimental models of inflammation. Oral administration of gall extract significantly inhibited carrageenan, histamine, serotonin and prostaglandin E2 (PGE2) induced paw edemas, while topical application of gall extract inhibited phorbol-12-myristate-13-acetate (PMA) induced ear inflammation. The extract also inhibited various functions of macrophages and neutrophils relevant to the inflammatory response(Wasim Ahmad *et al*, 2016).

Antimicrobial

In vitro antibacterial activity of methanol & aqueous extract of galls against several bacterial pathogens of the urinary tract infection was evaluated using disc diffusion method at the concentration of 5 mg/disc. Both the extracts showed similar inhibitory effects against 4 Gram-positive bacteria (*Staphylococcus saprophyticus, Streptococcus agalactiae, Streptococcus pneumonia*and *Enterococcus faecalis*) and a Gram-negative bacteria *Proteus mirabilis*. It has also been reported to be effective against *Escherichia coli, Staphylococcus aureus, Salmonella typhimurium, Pseudomonas aeruginosa*and *Bacillus subtilis* in another similar study.

Galls, at a concentration from 300, 600 and 1200 µg/ml exhibited a significant antibacterial effect expressed as minimum inhibitory concentration (MIC) against Gram-positive bacteria. In particular, *Staphylococcus aureus* and *Bacillus cereus* were the most inhibited. A study was carried out to evaluate the antimicrobial activity of the aqueous, ethanol and petroleum ether extracts of galls. The result reveals that the ethanol extract showed maximum inhibition against *Staphylococcus aureus, Escherichia coli, Pseudomonas aeruginosa*and*Candida albicans*.The antimicrobial activity of extracts of galls prepared from different solvents was evaluated against a wide variety of pathogenic bacteriasuch as *Escherichia coli*, *Staphylococcus aureus* and *Bacillus subtilis*by the discdiffusion method. All the extracts of galls exhibited a good antimicrobialactivitycompared to the commercial antibiotics. All the Gram-positive and all theGram-negative bacteria tested were susceptible to all the aqueous and solvent extracts of galls. Theactivity of differentextracts (petroleum ether, chloroform, methanol and water)of gallsagainst the dental pathogens like *Streptococcus mutans*,*Streptococcus salivarius, Staphylococcus aureus, Lactobacillus acidophilus*(designated) and*Streptococcus sanguis* (isolated) were evaluated. All the fourextracts inhibited the growth of all pathogens and methanolic extract was themost effective. The study concludes that Streptococcus sanguis showed greatersensitivity towards the methanolic extract. (Wasim Ahmad *et al*, 2016)

Antioxidant

Ethanolic extract of galls was investigated for its antioxidantactivity in vitro model systems. Its protective efficacy on oxidative modulation ofmurine macrophages was also explored. Galls extract was found to contain largeamount of polyphenols and possess a potent reducing power. The result concludedthat the galls possess potent antioxidant activity, when tested both in chemical aswell as biological models. A study was conducted to determine the antioxidant activity of galls, by using different in vitro methodologies. The antioxidant activity wasdetermined by the 2,2-diphenylpicrylhydrazyl (DPPH) assay and a â-carotenebleaching assay and compared with that of the butylatedhydroxyl toluene (BHT).The result showed that among aquatic, ethanolic and methanolic, extract ofgalls, water extract has high antioxidant activities. (Wasim Ahmad *et al*, 2016P)

2.1.6Long pepper*(Thippali)*

Botanical name*:* Piper longum

Parts use: Dry fruit

Active component

*Piper longum*contain piperine as the major and active constituent, thepiperine content is 3-5% (on dry weight basis) in Piper longum.The fruits gave positive result for presence of starch, protein and alkaloids, volatile oils, saponins, carbohydrates, and amygdalin and negative result for tannins (Dasgupta et al,1980).

Pharmacology:

Anti-apoptosis and antioxidant

The hexane: ethanol (2:8) extract of *Piper longum*shows anti apoptosis and antioxidant activity. The study accomplished that the fruit extract of *Piper longum*shows anti-apoptoss and antioxidant activity. (Dhanalakshmi*et al* 2016)

Anti-inflammatory and anti-arthritic activity

The fruit extract of *Piper longum*were reported to possess anti-inflammatory activity in carageanan rat paw edema. The aqueous extract of *piper longum*shows anti-arthritic effect on CFA (Complete Freuds Adjuvant) induced arthritis in rats. (Dhanalakshmi*et al* 2016)

Immunomodulatory activity

The immunomodulatory potential of *Piper longum*fruit extract have been evaluated by hoemagglutinationtitre(HA), macrophage migration index(MMI), and phagocytic index(PI) in mice. A familiar ayurvedic preparation containing long pepper, pippaliRasayana, was tested in mice infected with Giardia lamblia and found to produce significant activation of macrophages as shown by an increased MMI and phagocytic activity. (Dhanalakshmi*et al* 2016)

Anti-asthmatic activity

The ethanolic extract of *Piper longum*in milk reduced passive cutaneous anaphylaxis in rats and protected gunia pigs against antigen-induced bronchospasm(Dhanalakshmi*et al* 2016)

Anti-diabetic activity

Oral administration of dried fruits of *Piper longum*has shown significant anti-hyperglycemic, anti-hyperlipidemic effects in diabetic rats compared to that of the standard reference during glibenclamide (Dhanalakshmi*et al* 2016)

Anti-microbial activity

The fruit extract of *Piper longum*shown to possess anti-microbial activity against certain antibiotic resistant specific bacteria, this supports its traditional use as an anti-microbial remedy(Dhanalakshmi*et al* 2016)

Antidepressant activity

A bioassay guided isolation of the ethanolic extract from the fruit yielded a piperine alkaloid and piperine having potent antidepressant like activity, which are mediated in part through the inhibition of MAO activity. (Dhanalakshmi*et al* 2016)

Anti-amoebic activity

The methanolic extract of *Piper longum*fruit were tested for their efficacy against *Entamoebahistolytica*in vitro and against experimental cecalamebiasis in vivo. (Dhanalakshmi*et al* 2016)

Coronary vasodilation

The amide dehydropiperonaline analogue isolated from the fruit of *Piper longum*has demonstrated the ability to induce coronary vasodilation. (Dhanalakshmi*et al* 2016)

Anti-fungal activity

The essential oil isolated from the fruits of *Piper longum*showed fungicidal activity towards six phytopathogenic fungi, Pyriculariaoryzae, Rhizoctoniasolani, Botrytis cineria, Phytophthorainfestans, Pucciniarecondita, and Erysiphegraminis using a whole plant in vivo method. (Dhanalakshmi*et al* 2016)

Antiplatelet activity

The inhibitory effects of the four acid amides piperine, pipernonaline, piperoctadecalidine, and piperlongumine, isolated from the fruits of *Piper longum*Linn. were evaluated on washed rabbit platelet aggregation. These four tested acid amides dose-dependently inhibited washed platelet aggregation induced by collagen, arachidonic acid, and platelet-activating factor, but not that induced by thrombin. (Dhanalakshmi*et al* 2016)

3. CONCLUSION

By various literature searches it is well understood that each *K.M* formulas and its ingredients have good activity related to the management of pediatric for gastro intestinal problems, fever, cold, and skin diseases. This is an out layer review about the

pharmacological activities of the ingredients of *K.M.*According to our findings pharmacological properties of *K.M* is more effective on pediatric disease management.

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