A TOXICITY STUDY

ON

POORA PARPAM

Dissertation submitted to

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CONTENTS

INTRODUCTION ........................................................................................................ 2

REVIEW OF LITERATURE: .................................................................................. 6

CALOMEL: ........................................................................................................... 6

சுர்ருகமுருந்தோம்பை .................................................................................. 10

புருந் குர்கி பசவுகள் ............................................................................. 12

புருந் குர்கி பசவுகள் குட்டு .................................................................. 13

புருந் குர்கி பசவுகள் .......................................................................... 13

புருந் குர்கி பசவுகள் .......................................................................... 20

Piper Nigrum: ................................................................................................. 21

பிரிக் கேம்பை ......................................................................................... 22

பிரிக் கேம்பை ......................................................................................... 22

Curcuma Longa(பசச் மாக்கள்) ................................................................. 23

MECHANISAM OF ACTION ............................................................................... 24

மாற்றும் முறை ......................................................................................... 28

MERCURY-TOXICOLOGY: .............................................................................. 29

PHARMOCOKINETICS OF MERCURY EXPOSUERE .................................. 35

AIM AND OBJECTIVES .................................................................................. 44

AIM .................................................................................................................. 44

OBJECTIVE .................................................................................................. 44

MATERIALS AND METHODS ........................................................................ 46

MATERIALS REQUIRED: ............................................................................. 46

Purification ..................................................................................................... 46

Drug preparation .......................................................................................... 46

Toxicological study ...................................................................................... 46

Chemical analysis .......................................................................................... 46

METHODS ..................................................................................................... 47
LIST OF TABLES

Table 1: Properties of Calomel ................................................................. 6
Table 2: Chemical Constituents of Piper betel \cite{9} ........................................ 19
Table 3: Chemical Analysis of Poora Parpam .................................................. 53
Table 4: Test for Metals in Poora Parpam ...................................................... 54
Table 5: Acute Toxicity Study of Poora Parpam at Control ......................... 62
Table 6: Acute toxicity study at a dose of 40mg/100 gm body weight .......... 63
Table 7: Acute Toxicity Study at a dose of 80mg/100 gm body weight ........ 64
Table 8: Acute Toxicity Study at a dose of 160mg/100 gm body weight ....... 65
Table 9: Acute Toxicity Study at a dose of 320mg/100 gm body weight ...... 66
Table 10: Acute Toxicity Study at a dose of 640mg/100 gm body weight ...... 67
LIST OF FIGURES

FIGURE 1: துவக்கவுருக்கள்.......................................................... 43

FIGURE 2: DRUG PREPARATION 1 .................................................. ................................ 44

FIGURE 3: POORA PARPAM PREPARATION .................................................. .................. 45

FIGURE 4: FTISR RAW POORAM .......................................................... ................................ 55

FIGURE 5: FTISR PURIFIED POORAM.................................................. 55

FIGURE 6: FTISR POORA PARPAM.................................................. 56
INTRODUCTION
INTRODUCTION

Siddha system of medicine is commonly practiced by Tamilians of peninsular South India. Fundamental Principles of Siddha include theories of five elements (*Aimpootham*), and three humors (*Mukkuttram*). Siddha system of medicine not only includes polyherbal formulations, but also metals, chemicals, and/or animal products. The common Siddha preparations are parpam (calcined metals and minerals), Chenduram (red coloured powders), Churanam (powders), Kashayam (decoctions), Lehiyam (confections), Nei (ghee), Tailam (oil), and Mezhugu (wax). Calomel-containing preparations have been used extensively in siddha system of medicine for treatment of chronic ailments like syphilis, high fever, pneumonia, insomnia, nervous disorders, deafness, and paralysis of the tongue. Contrary to Western medicine, which does not promote the use of mercury due to its toxic effects, Siddha medical practitioners believe that mercury-based formulations have potent therapeutic efficacy, while there is no toxicity due to the unique and repeated purification processes employed during preparation.

However, lack of proper pharmacovigilance and widespread self-medication has resulted in undesirable effects to certain sections of the consumers of these preparations, which have contributed to the negative publicity for these forms of medicine. Variations in the quality of the preparations coupled with the lack of understanding of the differences in the recommended dosages and treatment strategies adopted by traditional medicine practitioners, further fuels concerns in the Western world on the safety and efficacy of traditional medicine. But in spite of these concerns, concerted efforts to understand the biological interactions and transformations of these preparations are yet to gain momentum. Although scattered reports on the toxicity of these preparations are available in literature, their mechanism of action has not been conclusively established. Long-term
pharmacotherapeutic and in-depth toxicity studies are needed to address the apprehensions raised by these herbo-metallic preparations.

This research work aims in evaluating the toxicological effects of Pooraparpam (ருபர்பம்)- calomel derived drug in albino rats. Calomel was taken internally and used as a laxative and disinfectant, as well as in the treatment of syphilis, until the early 20th century. Until fairly recently it was also used as a horticultural fungicide, most notably as a root dip to help prevent the occurrence of clubroot amongst crops of the Brassicaceae family.\[3\]

Calomel was used by doctors in America throughout the 18th century, and during the revolution, to make patients regurgitate and release their body from "impurities". Benjamin Rush was one particular well-known advocate of mercury in medicine and used calomel to treat sufferers of yellow fever during its outbreak in Philadelphia in 1793. Calomel was given to patients as a purgative or cathartic until they began to salivate and was often administered to patients in such great quantities that their hair and teeth fell out.\[4\] Shortly after yellow fever struck Philadelphia, the disease broke out in Jamaica. A war of words broke out in the newspapers concerning the best treatment for yellow fever; bleeding or calomel. Anecdotal evidence indicates calomel was more effective than bleeding.\[5\]

Pooraparpam is a calomel-derived drug widely used in therapeutic management of various skin disorders, venereal diseases, metabolic disorders and menstrual disorders. Its use has been described by many sages for treatment of various metabolic disorders including diabetes \[6\]. In siddha system of medicine calomel is used internally and externally for treatment of various genital cancers (செருநாய் பண்டும்பொய் சிலிக்கு பண்டு) and syphilitic ulcers (சுப்பிலிக் சி்த்பு) \[6\].
Though there are lot of methods described by various sages for preparation of pooraparpam, preparation using piper beetle and crab extract described in Aruvaimaruthuvam is followed in this research work.
REVIEW
OF
LITERATURE
REVIEW OF LITERATURE:

CALOMEL:

Mercury(I) chloride is the chemical compound with the formula Hg₂Cl₂. Also known as calomel (a mineral form, rarely found in nature). Mercurous chloride, this dense white or yellowish-white, odourless solid is the principal example of a mercury(I) compound. Various properties of calomel are shown in Table.2.1.

Table 1: Properties of Calomel

<table>
<thead>
<tr>
<th>Properties</th>
<th>Hg₂Cl₂</th>
</tr>
</thead>
<tbody>
<tr>
<td>Molecular formula</td>
<td>Hg₂Cl₂</td>
</tr>
<tr>
<td>Molar mass</td>
<td>472.09 g/mol</td>
</tr>
<tr>
<td>Appearance</td>
<td>White solid</td>
</tr>
<tr>
<td>Density</td>
<td>7.150 g/cm³</td>
</tr>
<tr>
<td>Melting point</td>
<td>525 °C (triple point)</td>
</tr>
<tr>
<td>Boiling point</td>
<td>383 °C (sublimes)</td>
</tr>
<tr>
<td>Solubility in water</td>
<td>0.2 mg/100 mL</td>
</tr>
<tr>
<td>Solubility</td>
<td>insoluble in ethanol, ether</td>
</tr>
<tr>
<td>Refractive index</td>
<td>1.973</td>
</tr>
</tbody>
</table>

புரள்:

புரளின் தென்கர் பாதி கிளிக் மெர்கூரியின் கம்பிப்பாக்கல் கருதிகான தின்மகாலம்.

புரளின் வரும் பாதி:

"குண்டுக்கள் கண்டத்து பரிசுபுரைகள் காணப்படுநாள்..."

- காலக்குமார், பக்கம் 29

"குண்டுக்கள் காணப்படுநாள்..."

- காலக்குமார், பக்கம் 76
புதுக்கோட்டை 64 - மாநாட்டுச்செல்வர் - பொருளாகம்பிள்ளைகள். இடையிலான 
மக்கள்துறையின் பொருளாகம் பல்கலை நூற்றாண்டுகள் காண்பதைத் தெளிவாக, வீட்டு விளையாட்டில் பொருள்பாடு நோங்காதே.

புதுக்கோட்டை செல்வர் - வீட்டு, காண்பு

குறிப்பிட்டு - மேம்பாடு

பிரிவு - காண்பு

சுதையாப்புக் கோடை, பாரைத்தை கோடை

அக்காலவடையும் பாடல்களைக் கோனி - பிள்ளைகள்

நாட்டுத் தொழில் முனைவர் பாடல்களின்

நூற்றாண்டு விளையாட்டுகள்

கொன்று விளையாட்டுகளில் அதைவு கோடை வீட்டுகள் பல்கலை நூற்றாண்டுகள் காண்பதைத் தெளிவாக, வீட்டு விளையாட்டில் பொருள்பாடு செய்யப்பட்டுள்ளது.

“செல்வர் தொடர் கோதி காலத்தால் காண்பாரம்

பிைலைதோ வளபைர் பெளித்தீர்க் குழந்தை

மீத்தை கிளைப்பிள்ளல் பார்வை கா் பூன்றை,

மீத்தை பிள்ளை ஆல் திருமை நூற்றாண்டு பாடல்”

திருகால பார்வையில் வாழ்க் காலத்தால் கோதி செல்வரின் விளையாட்டு

பாலன்களில் தோத்து பார்வையில் மாணவர் குழந்தை

பாலன்களில் பார்வையில் பிள்ளை காலத்தால் திருமை பாடல்

திருகால பார்வையில் பாலன்களின் விளையாட்டு கோதி பார்வையில்

கறை, பாலன்களில், பிள்ளை திருமை, காலத்தால், பிள்ளை காலத்தால், காலத்தால், பிள்ளை காலத்தால், பிள்ளை காலத்தால், பிள்ளை காலத்தால், பிள்ளை காலத்தால்.
பதானசீனம்: சிறுகோலைதூரில்

பாகானியப் பார்வோனேடு

பாகானியப் பார்வோனேடு

சிறுகோலைதூரில் பார்வோனேடு

முதுவானியப் பார்வோனேடு

பாகானியப் பார்வோனேடு

முதுவானியப் பார்வோனேடு

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முதுவானியப் பார்வோனேடு

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சிறுகோலைதூரில் பார்வோனேடு

முதுவானியப் பார்வோனேடு

சிறுகோலைதூரில் பார்வோனேடு

முதுவானியப் பார்வோனேடு
சுருக்கப்பட்டு அடிப்படை விளக்கம்

குறிப்பிட்டிய தமிழ் வரலாற்றின் வருமானத்தை நம்பிக்கை முறுக்கும் விளக்கம்

மற்றும் நம்பிக்கை முறுக்கும் விளக்கம்

தமிழ் அழகு உண்மையிலும் குறிப்பிட்டிய விளக்கம்

குறிப்பிட்டிய விளக்கம்

வேள்வியான பாணியில் நம்பிக்கை முறுக்கும் விளக்கம்

அனுப்பிய விளக்கம்

அனுப்பிய விளக்கம்
பூந்தான் (சின்னக்கோயம்)

புத்தவேண் – விபவான்

1. பாரம்பரியத்தில் 16  வகைகளில்  (627 கிரா) குற்றவாய் வெளிப்புறச்செய்திகள், 80 வகைகளில் (336 கி.மீ.) பச்சையூறுத் தொடருக்கு தொடருக்கு உறுதிச்செய்திகள் குற்றவாய் வெளிப்புறசெய்திகளுக்கு ஒத்துடன் பூந்தான், அதாவது, அல்லப்பு வரையில் (650 பிசிட்டர்கள்) குற்றவாய் வெளிப்புறசெய்திகள், பெரும்பானைச் செய்திகளுக்கு ஒத்துடன் 12 வகைகளைக் கொண்டு, அவைகள் குற்றவாய் வெளிப்புறசெய்திகளை உறுதிச்செய்திகளை குற்றவாய் வெளிப்புறசெய்திகளை உறுதிச்செய்திகளை உறுதிச்செய்திகளை உறுதிச்செய்திகளை உறுதிச்செய்திகளை உறுதிச்செய்திகளை உறுதிச்செய்திகளை உறுதிச்செய்திகளை உறுதிச்செய்திகளை உறுதிச்செய்திகளை உறுதிச்செய்திகளை உறுதிச்செய்திகளை உறுதிச்செய்திகளை உறுதிச்செய்திகளை உறுதிச்செய்திகளை உறுதிச்செய்திகளை உறுதிச்செய்திகளை உறுதிச்செய்திகளை உறுதிச்செய்திகளை உறுதிச்செய்திகளை உறுதிச்செய்திகளை உறுதிச்செய்திகளை உறுதிச்செய்திகளை உறுதிச்செய்திகளை உறுதிச்செய்திகளை உறுதிச்செய்திகளை உறுதிச்செய்திகளை உறுதிச்செய்திகளை உறுதிச்செய்திகளை உறுதிச்செய்திகளை உறுதிச்செய்திகளை உறுதிச்செய்திகளை உறுதிச்செய்திகளை உறுதிச்செய்திகளை உறுதிச்செய்திகளை உறுதிச்செய்திகளை உறுதிச்செய்திகளை உறுதிச்செய்திகளை உறுதிச்செய்திகளை உறுதிச்செய்திகளை உறுதிச்செய்திகளை உறுதிச்செய்திகளை உறுதிச்செய்திகளை உறுதிச்செய்திகளை உறுதிச்செய்திகளை உறுதிச்செய்திகளை உறுதிச்செய்திகளை உறுதிச்செய்திகளை உறுதிச்செய்திகளை உறுதிச்செய்திகளை உறுதிச்செய்திகளை உறுதிச்செய்திகளை உறுதிச்செய்திகளை உறுதிச்செய்திகளை உறுதிச்செய்திகளை உறுதிச்செய்திகளை உறுதிச்செய்திகளை உறுதிச்செய்திகளை உறுதிச்செய்திகளை உறுதிச்செய்திகளை உறுதிச்செய்திகளை உறுதிச்செய்திகளை உறுதிச்செய்திகளை உறுதிச்செய்திகளை உறுதிச்செய்திகளை உறுதிச்செய்திகளை உறுதிச்செய்திகளை உறுதிச்செய்திகளை உறுதிச்செய்திகளை உறுதிச்செய்திகளை உறுதிச்செய்திகளை உறுதிச்செய்திகளை உறுதிச்செய்திகளை உறுதிச்செய்திகளை உறுதிச்செய்திகளை உறுதிச்செய்திகளை உறுதிச்செய்திகளை உறுதிச்செய்திகளை உறுதிச்செய்திகளை உறுதிச்செய்திகளை உறுதிச்செய்திகளை உறுதிச்செய்திகளை உறுதிச்செய்திகளை உறуதி
1. கமாவைல், மிளவைக் (8.75 கிலோ) பெருசியில் புதுக்குள்ளையில் அடைக்கப் பெருமையான (1.3 கிலோ) பெருமையான குழுக்கள் அளிப்பாக செய்தன. பெருமையான குழுக்கள் பெருமையான புதுக்குள்ளையில் அடைக்கப் பெருமையான குழுக்கள் அளிப்பாக செய்தன. 

2. புதுக்குள்ளையில் புதுக்குள்ளையில் (35 கிலோ) பெருமையான குழுக்கள் பெருமையான குழுக்கள் அளிப்பாக செய்தன.

3. புதுக்குள்ளையில் புதுக்குள்ளையில் (35 கிலோ) பெருமையான குழுக்கள் அளிப்பாக செய்தன.

4. புதுக்குள்ளையில் புதுக்குள்ளையில் (35 கிலோ) பெருமையான குழுக்கள் அளிப்பாக செய்தன.

- கூட்டுமுனைப்பகுதியில்

- ஆராய்ச்சிப் பொறியியல் - 91

புதுக்குள்ளையில் பொறியியல்

புதாரம்:

குழுக்களில் பொறியியல் குழுக்கள் செய்யும் குழுக்களை கணித்துக்காண்க. இது முக்கியமான காலனித்துறைகளுக்கு வேண்டும்.
அளருந்து (32 மிக்க) போன்றவற்றில் கூட்டப்பட்டுள்ளது (195மிக்க) மற்றும் பாதுகாப்புக்கான விளைப்புக்குடி (130 மிக்க) கூட்டப்பட்டுள்ளது போக்குகாண்டுப் போக்குகள்.

ஒட்டசாரானது சுருக்கப்படும்.

குறுப்போக்குப் புரோப்புக்கான விளைப்புக்கான விளைப்புக் கூட்டப்பட்டுள்ளது.

புதுப்போக்குப் பயிற்சிகள்

போர்னூல் பயிற்சிகள்

ஏற்காட்டில் போர்னூல் பயிற்சிகள் கூறியிட்டுள்ளது. நூற்றாண்டுக்கு முன் போர்னூல் பயிற்சிகள் கூறியிட்டுள்ளது.

புதுப்போக்கு

சுருக்கம் (35 மிக்க) புராணம், பாதுகாப்புக்கான விளைப்புக்கான விளைப்புக் கூட்டப்பட்டுள்ளது.
தினம் இரண்டு:

துக்க அம்மனருக்கு சாதன செய்யவும் இழைக்கு வருவதும், நலனும். மலவாதுக்கு ஹிருக்க.

புத்தகம்

வாழ்போக்கள், கயங்கள் விளக்கமைப்பதற்கு ராணு உரைக்கார். இருபது (35 கிரா) புத்தகரையில் ராணு கையில், கூறுக்கு விளக்கமாக உரைக்கு வருகிறது.

புத்தகம் (வெளியிட்டு)

பொருட்பாடையில், கைகளில், பொருட்பாட்டு விளக்கமும் கூறு அணைகக்கு விளக்கமும். விளக்க பொருட்பாடு அணைகக்கு கட்டுப்பாட்டு குறுக்கு விளக்கமும், குறுக்கு கூறுக்கு விளக்கம் வருகிறது வருகிறது ஓரும் தொடரும் பொருட்பாடையில் கூறுக்கு விளக்கம் வருகிறது வருகிறது.

புத்தகம் குறிப்பிட்டு வரிசை:

(பொருட்பாடையில் வெளியிட்டு கால் வரிசை புது கால் வாக்கிலூடு (21 கிரா) பொருட்பாடையில் பொருட்பாடையிலூடு 20 வாக்கிலூடு (84 கிரா) பொருட்பாடையிலூடு 30 வாக்கிலூடு, பொருட்பாடையிலூடு 40 வாக்கிலூடு வாக்கிலூடு வாக்கிலூடு வாக்கிலூடு வாக்கிலூடு) வாக்கிலூடு. காலம்-காலம் பொருட்பாடையிலூடு பொருட்பாடையிலூடு வாக்கிலூடு.

அந்தப்

ஓர் பொருட்பாடையில் விளக்கமாக கூறு வருகிறது.

புத்தகம்

சமூக, பொருட்பாடையிலூடு.

சுற்று பொருட்பாடையிலூடு வாக்கிலூடு வாக்கிலூடு. கூறு காலம் வாக்கிலூடு பொருட்பாடையிலூடு பொருட்பாடையிலூடு. கூறு வாக்கிலூடு வாக்கிலூடு வாக்கிலூடு. கூறு வாக்கிலூடு வாக்கிலூடு.
கல்லூரியாளரின் கல்வியை செய்யும் தொடர: நூற்றாண்டு

<table>
<thead>
<tr>
<th>கல்வி வகுப்பு</th>
<th>பகுதி எண்</th>
</tr>
</thead>
<tbody>
<tr>
<td>அரசு பத்தாண்டு</td>
<td>88</td>
</tr>
<tr>
<td>இரண்டாம் பத்தாண்டு</td>
<td>114</td>
</tr>
<tr>
<td>முதலாம் பத்தாண்டு</td>
<td>150</td>
</tr>
</tbody>
</table>

முழு மாணுவகளின் புது விளக்கத்தில் கூற்றிய பகுதியைப் பிரிக்கும்.

கிளைக்கால நூற்றாண்டு கல்வி

1. பிற்காலக் கயிறாள் - பகுதி 110
2. தர்க்காரன் பாத்திரிகள் - பகுதி 129
3. இருப்பிட்ட பாத்திரிகள் - பகுதி 138
4. குறும்பு பாத்திரிகள் - பகுதி 141
5. சிற்று பாத்திரிகள் - பகுதி 142
6. நிற்குகாண்டுப் பாத்திரங்கள் - பகுதி 184
7. தேர்வு வால் குறிப்பு - பகுதி 185
8. குறிப்பிட்டு குறிப்பு - பகுதி 188
9. வேறுப்பு குறிப்பு - பகுதி 194
10. குறிப்பிட்டு குறிப்பு - பகுதி 197
11. பிறிதூணக் குறிப்பு - பகுதி 199
12. விளக்க குறிப்பு - பகுதி 237
13. நூற்றாண்டு குறிப்பு - பகுதி 242
14. வேறுப்பு குறிப்பு - பகுதி 247
15. பாதுகாக்கும் வேறுப்பு - பகுதி 260
16. தேவதை மையங்கள் - பகுதி 261
17. குறிப்பிட்டு வேறுப்பு - பகுதி 265
18. வேறுப்பு வேறுப்பு - பகுதி 270
19. பாதுகாக்கும் வேறுப்பு - பகுதி 293
20. வைத்திருவிளையாட்டு - பக்கம் 304

பம்பக் மாற்றக்கூடிய பகுதியின் வரையறை

பஞ்சார் சிற்றுறவு மான்னிக்குறிச் புரட்சியை - சேவீசு கல்வி 600 கால் குறிப்பிட்டு

............. குறிப்பிட்டு புரட்சி வசதிகளை பல்வேறு வசதிகளை பல்வேறு வசதிகளை

1. புரட்சி கல்வி - பக் 36
2. புரட்சி வசதி - பக் 38

பம்பக் மாற்றக்கூடிய புரட்சி வரையறை குறிப்பிட்டு

பஞ்சார் கல்வி கல்வி குறிப்பிட்டு

"தொலைதொலை விளையாட்டு புரட்சியை....." என்பது பாணா பாக்கக்குறிக்குப் பல்வேறு வசதிகளை

சேவீசு விளையாட்டு கல்வி 360 கால் குறிப்பிட்டு - பக்கம் 164

புரட்சி பக்கம்

சேவீசு புரட்சி பல்வேறு வசதிகளை

புரட்சி விளையாட்டு கல்வி - பக்கம் 3821

"தொலைதொலை விளையாட்டு பல்வேறு வசதிகளை

சேவீசு விளையாட்டு வசதிகளை

தொலைதொலை விளையாட்டு வசதிகளை
முரசுச் விளக்கம் தொன்றியைத் தைத்தியதால்

புத்தான் விளக்கம் குறிப்பிட்டுதலால்

வைத்துள்ள விளக்கம் தொடுமை புகை நூறு விளக்குத்திக்கு மேல் மொனாள் பாக்கிருந்து.

நான்கு விளக்கங்கள் - நம்பிக்கை நூறு என்பதால்

சதுரம் பெருமையறு விளக்கம் - பக்கம் 3

மூட்டு விளக்கம் - பக்கம் 4

தேர்தல் விளக்கம் - பக்கம் 8

சதுரம் விளக்கம் - பக்கம் 4

புத்தான் மூழ்குத்திகளின் புகை நூற்றாண்டு தேவியைப் பிள்ளை.
Piper betel:
Since antiquity, Piper betel Linn (betel vine; family Piperaceae) has been an important medicinal agent in the various traditional and folk systems of medicine in Southeast Asian countries. The leaves are the most valued plant part and in the past were routinely used as a chewing agent to prevent halitosis. The leaves are also supposed to harden the gum, conserve the teeth and to prevent indigestion, bronchitis, constipation, congestion, coughs and asthma. Innumerable scientific studies have
validated the ethno medicinal claims. Betel leaves are an integral component of the betel quid that consists of areca nut (Areca catechu Linn.), tobacco (Nicotianatabacum L) and slaked lime; a highly abused agent with carcinogenic properties. Regular chewing of betel quid is associated mainly with oral cancer and detail studies with individual constituents of the quid have shown that both tobacco and areca nut are carcinogenic, while slaked lime is shown to promote the process of carcinogenesis.

Table 2: Chemical Constituents of Piper betel[9]

<table>
<thead>
<tr>
<th>S.No</th>
<th>Compound</th>
<th>Activity</th>
<th>Mode of action</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Hydroxy-chavicol</td>
<td>Hyperuremia (antidiabetic), immunomodulatory, inhibits platelet aggregation</td>
<td>A potent COX-1/COX-2-inhibitors, ROS scavenging and inhibits platelet calcium signaling, TXB production and aggregation</td>
</tr>
<tr>
<td>2</td>
<td>Allylpyrocatechol</td>
<td>Gastric ulcer healing action, anti-inflammatory effect</td>
<td>Inflammatory response of macrophages via inhibition of iNOS, COX-2 and IL-12 p40 through down regulation of the NFkappaB pathway</td>
</tr>
<tr>
<td>3</td>
<td>Chavibetol</td>
<td>Radioprotective activity</td>
<td>Protects photosensitization-mediated lipid peroxidation of rat liver</td>
</tr>
<tr>
<td>4</td>
<td>Piperbetol</td>
<td>Platelet hyperactivity</td>
<td>Selectively inhibits platelet aggregation factor</td>
</tr>
</tbody>
</table>

However unlike other constituents of the betel quid, the betel leaves devoid carcinogenic effects and on the contrary possesses cancer preventive effects including against the carcinogens present in tobacco. Subsequent studies have conclusively
shown that the betel leaf and some of its phytochemicals also prevented chemical induced cancers in experimental animals\[^8\].

The main chemical constituents of piper betel leaves include Hydroxychavicol (HC)/ Hydroxychavicol acetate(HCA), Allylpyrocatechol (APC), Chavibetol (CHV), Piperbetol, arecoline, carvacrol, caryophyllene, piperitol, piperbetol, eugenol, isoeugenol, allylpyrocatechol, chavicol, safrole, anethole. Chavibetol, cadinene. Hydroxychavicol, β-sitosterol, β-sitostereypalmitate, dotriacontanoic acid, tritriacontane, stearic acid, cephadriodine, piperine, piperlonguminine. Chavibetol acetate, allylpyrocatecholmonoacetate.allyldiacetoxy benzene.estragole, methyl eugenol and hydroxycatechol.methylpiperbetol, piperol A and piperol B. cavaacrol, eugenol acetate, and allylpyrocatecholdiacetate\[^9\].

தமிழில் பொருள் -

பெரும்பாலான பொதுமக்களுக்கும் பொருளாக்களின் திறன்களையும் பதிக்கப்பட்டுள்ளது. இது வெவ்வேறு சமயங்களில் பயன்படுத்தப்படும் ஒரு செயலாகும்.

“தமிழ் வடிவில் அற்றவலைகள் அறிச்சூட்டுக் கொள்ளத்தேனால். ஐயைருந்து காள்ளினால்கூடாளும் கொள்ளத்தேனால். அல்லது பூட்டினால் கொள்ளத்தேனால்.”

- செய்திகள்தமிழில்

பெரும்பாலான பொது பொருளாக்களின் திறன்களையும் பதிக்கப்பட்டுள்ளது, இனான, அன்பிழியாய்க்கர், காள்ளினால். பின்பிட்டு தலைப்பாக வந்து அருகிப்பட்டிருந்த கொள்ளத்தேனால். காள்ளினால். விளையாட்டு பக்கத்தேனால்.

பின்பிட்டு செய்திகள்: காள்ளி

- தமிழகத்தில் பெரும்பாலான பொது பொருளாக்களின் திறன்களை பதிக்கப்பட்டுள்ளது. காள்ளினால் தமிழ்நாட்டில். ஆனானது பொருளாக்களின். விளையாட்டு பொருளாக்களின். அமைச்சரமாக பொருளாக்களின். விளையாட்டு பொருளாக்களின்.
**Piper Nigrum:**

Black pepper (*Piper nigrum*) is a flowering vine in the family Piperaceae, cultivated for its fruit, which is usually dried and used as a spice. The fruit, known as a peppercorn when dried, is approximately 5 millimetres (0.20 in) in diameter, dark red when fully mature, and, like aldrupes, contains a single seed. Peppercorns, and the powdered pepper derived from grinding them, may be described simply as pepper or more precisely as black pepper (cooked and dried unripe fruit), green pepper (dried unripe fruit) and white pepper (dried ripe seeds).

Black pepper is native to south India, and is extensively cultivated there and elsewhere in tropical regions. Currently Vietnam is the world's largest producer and exporter of pepper, producing 34% of the world's *Piper nigrum* crop as of 2008.

Dried ground pepper has been used since antiquity for both its flavour and as a medicine. Black pepper is the world's most traded spice. It is one of the most common spices added to European cuisine and its descendants. The spiciness of black pepper is due to the chemical piperine. It is ubiquitous in the industrialized world, often paired with table salt.

*Piper nigrum*, commonly is used as a stimulant and carminative and prescribed for cholera, dyspepsia, flatulence, diarrhoea and various gastric ailments. Several alkaloids and non-alkaloidal constituents have been reported from this plant. More than 40 compounds has been isolated from *piper nigrum*.

**மிளகிெப ைம:**

“த(யாகிெயG.திEIமைதயாவ”
பார்த்தையில் பாட்டுகள் வழக்கம் மூழ்கும் நல்லது கற்கல்

காரணமாக பாடலும் போது கற்கல் பாடல் வழியாக தரவு செய்யும் வாதங்களை துளையா தரும்போது குறிப்பிட்டாலே நன்றாக இருக்கும் வாதமும் இருக்கும். எனவே வாதம் தொடர்புடைய பொருளை அதிகரித்து வாதமே அதிகரித்து வாதமும் வழக்கமே வழக்கமே வழக்கமே வழக்கமே வழக்கமே வழக்கமே வழக்கமே வழக்கமே

வாதங்கள்:

1. வாதம் கொண்டு மூழ்கும் நல்லது பாடல் தொன்று அதிகங்களிலிருந்து விளைவான குறுக்கள் கற்கல் குறுக்கள் குறுக்கள் குறுக்கள் குறுக்கள் குறுக்கள் குறுக்கள்

2. வாதம் போர்த்து மூழ்கும் நல்லது பாடல் தொன்று அதிகங்களிலிருந்து விளைவான குறுக்கள் குறுக்கள் குறுக்கள் குறுக்கள் குறுக்கள் குறுக்கள்

3. வாதம் போர்த்து மூழ்கும் நல்லது பாடல் தொன்று அதிகங்களிலிருந்து விளைவான குறுக்கள் குறுக்கள் குறுக்கள் குறுக்கள் குறுக்கள்

4. வாதம் போர்த்து மூழ்கும் நல்லது பாடல் தொன்று அதிகங்களிலிருந்து விளைவான குறுக்கள் குறுக்கள் குறுக்கள் குறுக்கள் குறுக்கள்

5. வாதம் போர்த்து மூழ்கும் நல்லது பாடல் தொன்று அதிகங்களிலிருந்து விளைவான குறுக்கள் குறுக்கள் குறுக்கள் குறுக்கள் குறுக்கள்

6. வாதம் போர்த்து மூழ்கும் நல்லது பாடல் தொன்று அதிகங்களிலிருந்து விளைவான குறுக்கள் குறுக்கள் குறுக்கள் குறுக்கள் குறுக்கள்
Curcuma longa, a perennial herb and member of the Zingiberaceae (ginger) family, grows to a height of three to five feet and is cultivated extensively in Asia, India, China, and other countries with a tropical climate. It has oblong, pointed leaves and funnel-shaped yellow flowers. The rhizome, the portion of the plant used medicinally, is usually boiled, cleaned, and dried, yielding a yellow powder. Dried Curcuma longa is the source of the spice turmeric, the ingredient that gives curry powder its characteristic yellow colour. Turmeric is used extensively in foods for its flavour and colour, as well as having a long tradition of use in the Chinese and siddha systems of medicine, particularly as an anti-inflammatory and for the treatment of flatulence, jaundice, menstrual difficulties, hematuria, hemorrhage, and colic. Turmeric can also be applied topically in poultices to relieve pain and inflammation. Current research has focused on turmeric’s antioxidant, hepatoprotective, anti-inflammatory, anticarcinogenic, and antimicrobial properties, in addition to its use in cardiovascular disease and gastrointestinal disorders[10].

Active Constituents:

The active constituents of turmeric are the flavonoid curcumin (diferuloylmethane) and various volatile oils, including tumerone, atlantone, and
zingiberone. Other constituents include sugars, proteins, and resins. The best-researched active constituent is curcumin, which comprises 0.3-5.4 percent of raw turmeric.

**Pharmacokinetics**

Pharmacokinetic studies in animals have demonstrated that 40-85 percent of an oral dose of curcumin passes through the gastrointestinal tract unchanged, with most of the absorbed flavonoid being metabolized in the intestinal mucosa and liver.

Due to its low rate of absorption, curcumin is often formulated with bromelain for increased absorption and enhanced anti-inflammatory effect.

**Mechanisms of Action**

**Antioxidant Effects**

Water- and fat-soluble extracts of turmeric and its curcumin component exhibit strong antioxidant activity, comparable to vitamins C and E. A study of ischemia in the feline heart demonstrated that curcumin pretreatment decreased ischemia-induced changes in the heart. An in vitro study measuring the effect of curcumin on endothelial heme oxygenase-1, an inducible stress protein, was conducted utilizing bovine aortic endothelial cells. Incubation (18 hours) with curcumin resulted in enhanced cellular resistance to oxidative damage.

**Hepatoprotective Effects**
Turmeric has been found to have a hepatoprotective characteristic similar to silymarin. Animal studies have demonstrated turmeric’s hepatoprotective effects from a variety of hepatotoxic insults, including carbon tetrachloride (CCl), galactosamine, acetaminophen (paracetamol), and Aspergillus aflatoxin. Turmeric’s hepatoprotective effect is mainly a result of its antioxidant properties, as well as its ability to decrease the formation of proinflammatory cytokines. In rats with CCl-induced acute and subacute liver injury, curcumin administration significantly decreased liver injury in test animals compared to controls. Turmeric extract inhibited fungal aflatoxin production by 90 percent when given to ducklings infected with Aspergillus parasiticus. Turmeric and curcumin also reversed biliary hyperplasia, fatty changes, and necrosis induced by aflatoxin production. Sodium curcuminate, a salt of curcumin, also exerts choleretic effects by increasing biliary excretion of bile salts, cholesterol, and bilirubin, as well as increasing bile solubility, therefore possibly preventing and treating cholelithiasis.

**ANTI-INFLAMMATORY EFFECTS**

The volatile oils and curcumin of Curcuma longa exhibit potent anti-inflammatory effects. Oral administration of curcumin in instances of acute inflammation was found to be as effective as cortisone or phenylbutazone, and one-half as effective in cases of chronic inflammation. In rats with Freund’s adjuvant-induced arthritis, oral administration of Curcuma longa significantly reduced inflammatory swelling compared to controls. In monkeys, curcumin inhibited neutrophil aggregation associated with inflammation. C. longa’s antiinflammatory properties may be attributed to its ability to inhibit both biosynthesis of inflammatory prostaglandins from arachidonic acid, and
neutrophil function during inflammatory states. Curcumin may also be applied topically to counteract inflammation and irritation associated with inflammatory skin conditions and allergies, although care must be used to prevent staining of clothing from the yellow pigment.

**ANTICARCINOGENIC EFFECTS**

Animal studies involving rats and mice, as well as in vitro studies utilizing human cell lines, have demonstrated curcumin’s ability to inhibit carcinogenesis at three stages: tumor promotion, angiogenesis, and tumor growth. In two studies of colon and prostate cancer, curcumin inhibited cell proliferation and tumor growth. Turmeric and curcumin are also capable of suppressing the activity of several common mutagens and carcinogens in a variety of cell types in both in vitro and in vivo studies. The anticarcinogenic effects of turmeric and curcumin are due to direct antioxidant and free-radical scavenging effects, as well as their ability to indirectly increase glutathione levels, thereby aiding in hepatic detoxification of mutagens and carcinogens, and inhibiting nitrosamine formation.

**ANTIMICROBIAL EFFECTS**

Turmeric extract and the essential oil of Curcuma longa inhibit the growth of a variety of bacteria, parasites, and pathogenic fungi. A study of chicks infected with the caecal parasite Eimera maxima demonstrated that diets supplemented with 1-percent turmeric resulted in a reduction in small intestinal lesion scores and improved weight gain. Another animal study, in which guinea
pigs were infected with either dermatophytes, pathogenic molds, or yeast, that topically applied turmeric oil inhibited dermatophytes and pathogenic fungi, but neither curcumin nor turmeric oil affected the yeast isolates. Improvements in lesions were observed in the dermatophyte- and fungi-infected guinea pigs, and at seven days post-turmeric application the lesions disappeared. Curcumin has also been found to have moderate activity against Plasmodium falciparum and Leishmania major organisms.

**CARDIOVASCULAR EFFECTS**

Turmeric’s protective effects on the cardiovascular system include lowering cholesterol and triglyceride levels, decreasing susceptibility of low density lipoprotein (LDL) to lipid peroxidation, and inhibiting platelet aggregation. These effects have been noted even with low doses of turmeric. A study of 18 atherosclerotic rabbits given low-dose (1.6-3.2 mg/kg body weight daily) turmeric extract demonstrated decreased susceptibility of LDL to lipid peroxidation, in addition to lower plasma cholesterol and triglyceride levels. The higher dose did not decrease lipid peroxidation of LDL, but cholesterol and triglyceride level decreases were noted, although to a lesser degree than with the lower dose. Turmeric extract’s effect on cholesterol levels may be due to decreased cholesterol uptake in the intestines and increased conversion of cholesterol to bile acids in the liver. Inhibition of platelet aggregation by C.longa constituents is thought to be via potentiation of prostacyclin synthesis and inhibition of thromboxane synthesis.

**GASTROINTESTINAL EFFECTS**
Constituents of Curcuma longa exert several protective effects on the gastrointestinal tract. Sodium curcuminate inhibited intestinal spasm and p-tolymethylcarbinol, a turmeric component, increased gastrin, secretin, bicarbonate, and pancreatic enzyme secretion. Turmeric has also been shown to inhibit ulcer formation caused by stress, alcohol, indomethacin, pyloric ligation, and reserpine, significantly increasing gastric wall mucus in rats subjected to these gastrointestinal insults[^10].

பகுதிகள்:

1. குர்கூமா 
2. வெள்ளைகள்

கலை: காழ்புடன்

குறிப்பிட்டு: குர்கூமா

பிரிவு: காழ்புடன்

மூலகம்: பெரிதுவடையும், காக்கூட்டுவடையும், குர்கூமாவடையும், ரைன்வடையும்

குறிப்பிட்டு: 

"துவக்காகியின் விளையாட்டு காண்பாட்டு விளைந்து
காழ்புடன் பெரிதுவடைக்கு தடைமறைவு
காழ்புடன் குர்கூமாவடையும்
குர்கூமாவடையும், மாணறை."
1. மருத்துவ வலுவானால் புனிதத்தில் பாதுகாக்க வேண்டும். அவர்கள் அழுது.
2. சாத்துக்கும் மருத்துவத்தில் பருவத்தில் அருகில் தலைகிண்ணில் பாதுகாக்கப்
போன அவர்கள் தீர்வாக்கப்படும்.

மருத்துவ- தாவர் இருந்து நீரில் பிறந்த நீர்

**MERCURY - TOXICOLOGY:**

Mercury is a heavy metal of known toxicity, noted for inducing public health
disasters. The clinical impact of smaller mercury exposures remains controversial. It
exists in several forms: inorganic mercury, which includes metallic mercury and
mercury vapour (Hg0) and mercurous (Hg2++) or mercuric (Hg++) salts; and organic
mercury, which includes compounds in which mercury is bonded to a structure
containing carbon atoms (methyl, ethyl, phenyl, or similar groups). The biological
behaviour, pharmacokinetics, and clinical significance of the various forms of mercury
vary with chemical structure. There is some inter conversion in vivo between the
various forms of mercury. Inhaled elemental mercury vapour, for example, is easily
absorbed through mucus membranes and the lung and rapidly oxidized to other forms
(but not so quickly as to prevent considerable deposition of elemental mercury in the
brain). Methyl mercury is easily absorbed through the gut and deposits in many
tissues, but does not cross the blood-brain barrier as efficiently as elemental mercury;
however, on entering the brain it is progressively demethylated to elemental mercury.
Mercury salts, in contrast, tend to be insoluble, relatively stable, and poorly absorbed.
Human toxicity varies with the form of mercury, the dose and the rate of exposure.
The target organ for inhaled mercury vapour is primarily the brain. Mercurous and
mercuric salts chiefly damage the gut lining and kidney, while methyl mercury is
widely distributed throughout the body. Toxicity varies with dosage: large acute
exposures to elemental mercury vapour induce severe pneumonitis, which in extreme
cases can be fatal. Low-grade chronic exposure to elemental or other forms of
mercury induces subtler symptoms and clinical findings, as discussed hereinafter.
There is considerable controversy about the clinical significance of exposure to the
various forms of mercury and some disagreement regarding techniques for clinical
assessment of mercury burden[12].

Mercury exists in nature primarily as elemental mercury or as a sulfide and is
found in the earth’s crust at approximately 0.5 parts per million. Atmospheric
exposures occur from outgassing from rock or through volcanic activity. Human
sources of atmospheric mercury include coalburning and mining (mercury and gold in
particular). Atmospheric elemental mercury settles in water, where it is converted by
microorganisms into organic (methyl or ethyl)mercury, which is ingested by smaller
creatures which are eventually consumed by larger fish. Fish at the top of the food
chain (e.g., tuna, swordfish, or shark) may concentrate considerable mercury in their
tissues. Human mercury exposures occur chiefly through inhalation of elemental
mercury vapour via occupational or dental amalgam exposure or through ingestion of
mercury bonded to organic moieties (methyl, dimethyl, or ethylmercury), primarily
from seafood. Most human metallic mercury exposure comes from mercury vapour
outgassing from amalgam fillings, at a rate of 2 to 28 micrograms per facet surface per
day, of which about 80% is absorbed, according to the World Health Organization. A
less common source of mercury vapour is spilled mercury, and there is a report in the
literature of Idiopathic Thrombocytopenic Purpura caused by vacuuming spilled
mercury (thereby producing a major acute exposure to mercury vapour). Methyl and
dimethyl mercury (organic mercury) usually originate from biological sources, chiefly
fresh or salt waterfish. Over three thousand lakes in the United States have been closed
to fishing due to mercury contamination and many species of ocean fish are also tainted with considerable concentrations of mercury\[^{13}\].

**PHARMACOKINETICS OF MERCURY EXPOSURE**

**Inorganic Mercury**

**Elemental or Metallic (Hg\(0\)) Mercury:** Approximately 80\% of metallic mercury vapour outgassed from amalgams is absorbed through inhalation, compared with about 7 to 10\% absorption of ingested metallic mercury, and about 1\% absorption of metallic mercury through skin contact. On entry to the body, mercury vapour has great affinity for sulfhydryl groups and bonds to sulfur-containing amino acids throughout the body. Mercury vapour is transported to the brain, either dissolved in serum or adherent to red cell membranes. Metallic mercury passes easily through the blood brain barrier and through the placenta, where it lodges in the fetal brain. Metallic mercury is, however, rapidly oxidized to mercuric mercury on entry to the blood stream, although not so quickly as to prevent considerable uptake by the central nervous system while still in the metallic form. In addition to the brain, metallic mercury is also deposited in the thyroid, breast, myocardium, muscles, adrenals, liver, kidneys, skin, sweat glands, pancreas, enterocytes, lungs, salivary glands, testes, and prostate and may be associated with dysfunction of those organs. Mercury also has affinity for binding sites on the surface of T cells and for sulfhydryl groups influencing T cell function. Mercury deposits readily in placenta and fetal tissues and is found in breast milk. Metallic mercury is largely excreted as mercuric mercury. The excretory half-lives of metallic and mercuric mercury vary widely, depending on the organ of deposition and redox state, with values ranging from a few days to several months,
with some pools (e.g., CNS) having a half-life exceeding several years. Hair mercury does not correlate with brain content of metallic mercury. These complexities make accurate assessment of body burden challenging\textsuperscript{[13]}.

**Mercurous (Hg\textsuperscript{2+}) Mercury:**

Mercurous mercury salt in the form of Hg\textsubscript{2}Cl\textsubscript{2} (calomel) is poorly soluble in water and poorly absorbed by the intestine, although some portion is thought to undergo oxidation to more readily absorbable forms. It is doubtful that mercurous mercury survives in the body, other than as a transitional form between metallic and mercuric mercury. Some absorption evidently occurs, however, as calomel is occasionally associated with pink disease, or acrodynia.

**Mercuric (Hg\textsuperscript{+}) Mercury:**

Historically, mercuric chloride (HgCl\textsubscript{2}) was used as a preservative and for development of photographic film and was ingested accidentally or as a suicide measure. It is a component of some skin-lightening creams. Only about 2% of ingested mercuric chloride is absorbed initially, although it is believed that its corrosive effect on the intestine may increase permeability and, hence, absorption, with prolonged exposure. Available data on skin penetration of mercuric mercury are insufficient to make quantitative comparison with ingestion or with metallic mercury. Like metallic mercury, mercuric mercury in the bloodstream adheres to sulfhydryl groups on erythrocytes, metallothionein, or glutathione or is suspended in plasma. Mercuric mercury does not cross the blood-brain barrier efficiently, but it does accumulate in quantity in the placenta, fetal tissues, and amniotic fluid. Evidence exists showing transport of mercuric mercury via one or more amino acid transporters, particularly that for cysteine, which may account for accumulation in the brain. Much of the body burden of mercuric mercury resides in the proximal
convoluted renal tubule bonded to metallothionein. Significant deposition also occurs periportally in the liver and lesser amounts in epithelial tissues, choroidal plexus, and testes. Excretion of mercuric mercury is largely through urine and stool, although significant amounts are shed through sweat, tears, breast milk, and saliva. Half-lives appear to be multiphasic, as with metallic mercury, with human studies suggesting an effective half-life of 42 days for 80% of an oral tracer dose; the other 20% did not appear to have a measurable rate of excretion. This may reflect demethylation to metallic mercury in the brain and other organs or mechanisms yet to be determined.

**Organic Mercury Compounds:**

Most available data on organic mercury compounds refer to methyl mercury, which is a major source of human mercury exposure, is found naturally in fish, and is relatively stable. Ethyl mercury behaves in a similar fashion to methyl mercury at the cellular level, but with an excretory half-life about one third as long. Methyl mercury vapour is absorbed with similar (80%) efficiency as metallic mercury vapour. Intestinal absorption of methyl mercury from fish is also fairly efficient, as is absorption through the skin. On entry to the bloodstream, methyl mercury adheres to sulphydryl groups, particularly to those in cysteine. Methyl mercury is deposited throughout the body, with equilibrium between blood and body occurring approximately four days after exposure. Distribution to peripheral tissues seems to occur through one or more transporters, especially the cysteine transporter, probably adherent to the sulphydryl group in cysteine. Concentration of methyl mercury occurs in the brain, liver, kidneys, placenta, and fetus, especially in the fetal brain, as well as in peripheral nerves and bone marrow. Deposited methyl mercury slowly undergoes
demethylation to inorganic mercury. The excretory half-life of methyl mercury in man is about 70 days, with approximately 90% being excreted in stool. Some degree of enterohepatic circulation apparently occurs. Perhaps 20% of methyl mercury is excreted in breast milk, with the actual amount varying with severity of exposure. Hair mercury reflects blood methyl mercury at the time of incorporation, but not elemental mercury, and hence is not a good index of total body burden, given the short half-life of methyl mercury in blood. Dimethyl mercury is also efficiently absorbed through the skin, and there is a reported death of a scientist caused by minimal skin contact\textsuperscript{13}.

**Toxicity**

**Inorganic Mercury**

**Metallic Mercury Vapour:**

Mercury in all forms poisons cellular function by altering the tertiary and quaternary structure of proteins and by binding with sulfhydryl and selenohydryl groups. Consequently, mercury can potentially impair function of any organ, or any subcellular structure. The chief target organ of mercury vapour is the brain, but peripheral nerve function, renal function, immune function, endocrine and muscle function, and several types of dermatitis have been described. With massive acute exposure to mercury vapour, erosive bronchitis and bronchiolitis potentially leading to respiratory failure may be accompanied by CNS symptoms such as astremor or erethism.

Chronic exposure to clinically significant doses of mercury vapour usually produces neurological dysfunction. At low-level exposures, nonspecific symptoms like weakness, fatigue, anorexia, weight loss, and gastrointestinal disturbance have been described. Higher exposure levels are associated with mercurial tremor: fine muscle fasciculations punctuated every few minutes by coarse shaking. Erethism may also be observed: severe behaviour and personality changes, emotional excitability, loss of
memory, insomnia, depression, fatigue, and in severe cases delirium and hallucination. Gingivitis and copious salivation have been described. These symptoms may regress with cessation of exposure, but in many cases do not. Persistent neurological symptoms are common.

**Mercurous Mercury:**

Calomel (Hg2Cl2) is still used in some regions of the world as a laxative. Although poorly absorbed, some is converted to mercuric mercury, which is absorbed and induces toxicity as expected with mercuric mercury.

**Mercuric Mercury:**

Acute poisoning with mercuric salts (typically HgCl2) generally targets the gastrointestinal tract and the kidneys. Extensive precipitation of enterocyte proteins occurs, with abdominal pain, vomiting, and bloody diarrhoea with potential necrosis of the gut mucosa. This may produce death either from peritonitis or from septic or hypovolemic shock. Surviving patients commonly develop renal tubular necrosis with anuria. Chronic poisoning with mercury salts is rare, usually also involving concomitant occupational exposure to mercury vapour. Kidney toxicity involves either renal tubular necrosis or autoimmune glomerulonephritis, or both. Immune dysfunctions include hypersensitivity reactions to mercury exposure, including asthma and dermatitis, various types of autoimmunity, and suppression of natural killer cells and disruption of various other lymphocyte subpopulations. Brain dysfunction is less evident than with other forms of mercury. Thyroid dysfunction seems associated with inhibition of the 5-deiodonases, with decreased free T3 and increased reverse T3. Accumulation in the testicles appears to inhibit spermatogenesis. Atrophy and capillary damage have been described in thigh muscle.
Organic Mercury:

Methylmercury reacts with sulfhydryl groups throughout the body, therefore potentially interfering with the function of any cellular or subcellular structure. Mercury is believed to interfere with DNA transcription and protein synthesis, including protein synthesis in the developing brain, with destruction of endoplasmic reticulum and disappearance of ribosomes. Evidence suggests disruption of numerous subcellular elements in the central nervous system and other organs and in mitochondria; adverse effects have also been described on heme synthesis, cell membrane integrity in many locations, free radical generation, neurotransmitter disruption, and stimulation of neural excitoxins, resulting in damage to many parts of the brain and peripheral nervous system. Methyl mercury has been associated with reduction in Natural Killer cell activity, as well as an imbalance Th2: Th1 ratios favouring autoimmunity.

Mercury is also possibly associated with disruption of DNA repair. The affinity of mercury for sulfhydryl groups of the mitochondrial oxidative phosphorylation complex associated with destruction of mitochondrial membranes may contribute to chronic fatigue syndrome.

5. Clinical Presentation

Inorganic

Elemental (Metallic) Mercury:

Acute exposure to a large quantity of mercury vapour induces pneumonitis, as discussed previously. Symptoms of low-grade chronic exposure are more subtle and nonspecific: weakness, fatigue, anorexia, weight loss, and gastrointestinal distress, sometimes referred to as micromercuralism. At higher exposures, the mercurial fine
tremor punctuated by coarse shaking occurs; erethism, gingivitis, and excessive salivation have also been described, as has immune dysfunction. Objective findings include altered evoked potentials and decreased peripheral nerve conduction velocity. Objective measures of short-term memory may be inversely correlated with urinary mercury in chloralkali workers. Reduced colour vision and visual acuity have also been observed. Changes in coordination, tremor, mental concentration capacity, facial expression, and emotional state are also described, as are polyarthritis, various forms of dermatitis, and a syndrome mimicking pheochromocytoma. Subtler clinical findings among dentists have been documented, including delayed reaction time, poor fine motor control, and deficits in mental concentration, vocabulary, task switching, and the One Hole test, as well as mood lability, all correlating with urinary mercury excretion. Evidence also links elemental mercury to depression, excessive anger, and anxiety, as well as acute myocardial infarction, lipid peroxidation, and carotid atherosclerosis, in Finland; the Finnish experience may possibly be explained by dietary selenium deficiency, since selenium antagonizes mercury toxicity. Other investigators, however, have described associations between mercury and hypertension, lipid peroxidation, ischemic heart disease, and stroke.[13]

**Mercuric Salts:**

Ingestion of mercuric chloride produces extensive precipitation of intestinal mucosal proteins, mucosal necrosis, generalized abdominal pain, bloody diarrhea, and shock. If the patient survives, acute renal failure may follow.

**Organic Mercury:**
Methyl mercury and ethyl mercury produce similar signs and symptoms. Most published data refer to methyl mercury. Symptoms relate more to magnitude of methyl mercury retention than to the rate of deposition. Acute exposures tend to have a latency period of one or more weeks; once acquired, toxic doses are cleared slowly, if at all. Massive prenatal poisoning may induce a form of cerebral palsy. Lesser prenatal doses have been associated with neuro-developmental delays and cognitive deficits. Postnatal exposures generate a range of symptoms ranging from paresthesias, with lesser exposures, to ataxia, visual, auditory, and extrapyramidal impairments with moderate exposures and clonic seizures in more severe exposures. Objective physical findings are similar to those seen with elemental mercury exposure.
Aim

and

Objectives
AIM AND OBJECTIVES:

AIM:
To purify calomel (ஹும்பு) and prepare Poora Parpam using traditional siddha methods with detailed study on acute and long term toxicity of “POORA PARPAM” in animal model (Wister albino rats)

OBJECTIVE:
1. Purification of POORAM using siddha literature
2. Preparation of POORA PARPAM using siddha literature
3. Chemical analysis of POORA PARPAM
4. Toxicity study on “POORA PARPAM” using animal models
   a. Acute toxicity
   b. Chronic toxicity
MATERIALS AND METHODS
MATERIALS AND METHODS:

MATERIALS REQUIRED:

PURIFICATION:

1. Calomel (கலோமேல்)
2. Piper betel (பிபர் பெடெல்)
3. Piper nigrum (பிபர் சிரெம்)
4. தாவராகி குளிங்குத்தி

DRUG PREPARATION:

1. Calomel (கலோமேல்)
2. Piper betel (பிபர் பெடெல்)
3. Boiled rice (முட்டிக்குளிங்குத்தி)
4. Curcuma aromatic (சூர்யை மாடான்)
5. Crab fat (சுந்தரிய கயர்)

TOXICOLOGICAL STUDY:

Animals - Wistar albino rats (200 ± 25 g) bred in the animal house of GSMC, palayamkottai, were used. The animals were housed in wire-bottomed cages under a uniform condition of temperature and humidity and fed with normal food and tap water.

Chemical analysis:

1. Ammonium oxalate
2. Barium chloride
3. Silver nitrate
4. Con. Hydro chloric acid
5. Iodine solution
6. Glacial acetic acid
7. Potassium ferro cyanide
8. Con. Nitric acid
9. Ammonium thiocyanate
10. Ammonium molybdate
11. Esbatch’s reagent
12. Ferric chloride
13. Potassium permanganate
14. Ninhydrin
15. Potassium ferrocyanide

METHODS:

PURIFICATION:

8.75g of leaves of piper betel leaves and 8.75g of black pepper are taken and grinded using water and is made in to a paste. This is then dissolved in 1.3L of water. This solution is kept in the lower vessel of Thulaenthiram (துலாந்திரம்).
A single piece of pooram weighing around 35g is then tied in a thread and is allowed to hang inside the vessel containing solution. The whole setup is the heated from below till the amount of solution is reduced to 1/4\textsuperscript{th} of the total amount. Then the pooram is washed and stored in a container.

**Drug Preparation:**

A single piece of purified pooram is taken and is completely covered with the mixture of boiled rice and turmeric. This is then kept in a clay vessel and is heated from below.

**Figure 2: Drug Preparation 1**

Heat should be applied till the outer covering gets blackish colour. Same procedure is repeated 10 times. Then the processed piece of pooram is heated in a clay pot and crab fat is applied on the pooram piece, so that the piece absorbs the poured crab fat. This process should be done continuously for 24 hours. This is then cooled, made in to fine powder and is stored.
Figure 3: Poora Parpam Preparation

TOXICOLOGY STUDY:

SELECTION OF ANIMAL SPECIES:

Usually animal experiments are conducted on mice, albino rats, rabbit and dog. Young and immature animals should be selected for the study. In case of albino rats, it should be 180-200gm weight and 12 weeks growth.

PREPARATION OF ANIMALS:

Animals should be properly caged and should be fed properly with adequate diet. Allow the animals to be in the cage for 5 days before drug administration, in order to make them accustomed to the new environment. The temperature maintained in the animal house should be 12 hours dark and the remaining 12 hours full of light. Only healthy animals should be selected for the study.
**PREPARATION OF THE DRUG:**

The drug used for animal study should be free from microbes. Highly irritant and highly toxic drugs should not be given to the animals. The drug must dissolve in any one of the suspending agents such as water, milk, honey, castor oil etc.

**PREPARATION OF DOSES:**

1. While doing animal study the dose of the drug given is determined on the basis of body weight of the animal.
2. In case of mice and albino rats, the dose of the drug must be 1 ml/100gm. body weight.
3. When water soluble drugs are given, it must be 2 ml/100 gm. body weight.
4. The adjuvant (அடுக்குக் கருப்பு) used should be free from toxic properties.

**ADMINISTRATION OF DRUG:**

During drug administration care should be taken that the drug does not enter into the respiratory passage. Before drug administration, the animal has to be fasted. In case of albino rats the fasting period is 12 hours. The weight of the animal has to be noted before drug administration. Then the drug is administered to the animal. Later the albino rats are fed with proper diet 1-2 hours and 3-4 hours respectively after drug administration.

**NUMBER OF ANIMALS AND DOSE LEVELS:**

The dose of the drug given to the animal depends upon.

1. Body weight of the animal
2. Metabolic rate of the animal
While conducting acute toxicity study the number of animals in each group should be 5+5. Animals of both sex should be used. In case of chronic toxicity study the animals are divided into 4 groups, each group consisting of 20+20 animals.

**Observation:**

In acute toxicity study, the animals are carefully observed during the first 30 minutes and then observed for 24 hours. During that period, the animal may show changes in the skin, eye, mucous membrane, blood circulation, respiratory movements and the neurological problems may arise.

In case of sub-acute toxicity study the animals have to be observed for 90 days or sometimes up to 1 year. Some researchers conduct the chronic toxicity study for the whole lifetime of the animal.

**Body weight of the animal:**

The weight of the animal must be taken four times during the course of study.

i. First before drug administration.

ii. One Week after drug administration.

iii. Two weeks after drug administration.

iv. Before sacrificing the animal.

**Data and report:**

At the end of the animal study, the following data must be given.

1. Number of animals selected for the study.

2. Number of animals died due to the toxicity of the drug given.

3. Number of animals sacrificed at the end of animal study.
4. Changes in animal behaviour due to acute and chronic toxicity.

5. Histo-pathological changes in the internal organs such as liver, kidney and heart.

**CHRONIC TOXICITY STUDY**

1. This experiment has to be carried out 90 days to one year or one year to five years or entire life span of the animal.

2. Observe the animal daily and record the findings observe for cumulative effect of toxicity.

**CHEMICAL ANALYSIS:**

**PREPARATION OF EXTRACT:**

100mgs of the drug is weighed accurately and placed in a clean beaker and few drops of Con. Hcl is added and allowed to evaporate. Then it is allowed to cool and few drops of Con. Nitric acid is added. It is then allowed to cool and 20ml of distilled water is added so that it gets dissolved in it. This is then transferred to 100ml volumetric flask and is made up to 100ml with distilled water. This is then mixed, filtered and is taken for analysis.

**TEST FOR CALCIUM:**

2ml of the extract is taken in a clean test tube and 2ml of 4% ammonium oxalate solution is added to it. Appearance of white precipitate indicates the presence of calcium.

**TEST FOR SULPHATE:**

2ml of the extract is added to 5% barium chloride solution. Appearance of white precipitate indicates the presence of sulphate.
TEST FOR CHLORIDE:

Extract is treated with silver nitrate solution. Appearance of white precipitate indicates the presence of chloride.

TEST FOR CARBONATE:

The substance is treated with concentrated hydrochloric acid. Appearance of brisk effervescence indicates the presence of sulphate.

TEST FOR STARCH:

The extract is added with weak iodine solution. Formation of blue colour indicates the presence of starch.

TEST FOR IRON:

The extract is acidified with glacial acetic acid and potassium ferrocyanate is added. Formation of blood red colour indicates the presence of ferrous iron.

TEST FOR PHOSPHATE:

The extract is treated with ammonium molybdate and concentrated nitric acid. Appearance of yellow precipitate indicates the presence of phosphate.

TEST FOR ALBUMIN:

Extract is treated with Esbatch’s reagent. Formation yellow precipitate indicates the presence of albumin.

TEST FOR TANNIC ACID:

The extract is treated with ferric chloride. Appearance of black precipitate indicates the presence of tannic acid.

TEST FOR UNSATURATION:

Potassium permanganate is added to the extract. Decolourisation of the solution indicates the presence of unsaturated fatty acids.
TEST FOR REDUCING SUGAR:

5ml of benedict’s solution is taken in a test tube and allowed to boil for 2 minutes. Then 8-10 drops of extract is added to it and is boiled for 2 minutes. Significant colour change indicates the presence of reducing sugar.

TEST FOR AMINO ACID:

One or two drops of the extract is placed on a filter paper and dried. After drying 1% Ninhydrin is sprayed over it and dried. Formation of violet colour indicates the presence of amino acid.

TEST FOR ZINC:

The extract is treated with potassium ferro cyanide. Appearance of white precipitate indicates the presence of zinc.
RESULTS
**RESULTS:**

**PURIFICATION:**

Weight of raw pooram – 200g

Weight of piper betel – 54g

Weight of piper nigrum – 54g

Amount of water – 6L

Weight of pooram after purification – 192g

The above data’s showed that their is loss of total of 8g from 200g of pooram taken for purification. Totally there is loss of 4% of raw drug after purification.

**POORA PARPAM – PREPARATION:**

Weight of purified Pooram – 192g

Amount of boiled rice – 250g

Amount of turmeric powder – 100g

Total No. of Crabs – 200 (6.5 kgs)

Weight of Poora parpam before grinding – 190g

Weight of Poora parpam after grinding – 185g

The above data’s indicate that 185g of pooraparpam is prepared from 192g of purified pooram with 3.2% weight loss.
Chemical Analysis:
Table 3: Chemical Analysis of Poora Parpam

<table>
<thead>
<tr>
<th>S.No</th>
<th>Substance</th>
<th>Result</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Calcium</td>
<td>+</td>
</tr>
<tr>
<td>2</td>
<td>Sulphate</td>
<td>+</td>
</tr>
<tr>
<td>3</td>
<td>Chloride</td>
<td>+</td>
</tr>
<tr>
<td>4</td>
<td>Carbonate</td>
<td>-</td>
</tr>
<tr>
<td>5</td>
<td>Starch</td>
<td>-</td>
</tr>
<tr>
<td>6</td>
<td>Ferric iron</td>
<td>-</td>
</tr>
<tr>
<td>7</td>
<td>Ferrous iron</td>
<td>+</td>
</tr>
<tr>
<td>8</td>
<td>Phosphate</td>
<td>-</td>
</tr>
<tr>
<td>9</td>
<td>Albumin</td>
<td>-</td>
</tr>
<tr>
<td>10</td>
<td>Tannic acid</td>
<td>-</td>
</tr>
<tr>
<td>11</td>
<td>Unsaturated compounds</td>
<td>+</td>
</tr>
<tr>
<td>12</td>
<td>Reducing sugar</td>
<td>-</td>
</tr>
<tr>
<td>13</td>
<td>Amino acid</td>
<td>-</td>
</tr>
<tr>
<td>14</td>
<td>Zinc</td>
<td>-</td>
</tr>
</tbody>
</table>

Data’s in the above table indicates that small amount of unsaturated compounds, ferrous iron, chloride, sulphate and calcium are present in Poora Parpam.
**Test for Metals:**

**Table 4: Test for Metals in Poora Parpam**

<table>
<thead>
<tr>
<th>S.No</th>
<th>Metals</th>
<th>Amount</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>As 193.696 (Arsenic)</td>
<td>BDL</td>
</tr>
<tr>
<td>2</td>
<td>Cd 226.502 (Cadmium)</td>
<td>BDL</td>
</tr>
<tr>
<td>3</td>
<td>Cu 324.754 (Copper)</td>
<td>BDL</td>
</tr>
<tr>
<td>4</td>
<td>Hg 253.652 (Mercury)</td>
<td>3.421mg/L</td>
</tr>
<tr>
<td>5</td>
<td>Pb 230.204 (Lead)</td>
<td>BDL</td>
</tr>
</tbody>
</table>

BDL = Below detection limit

The above data show that mercury is present in large quantity in the drug. But all other metals such as lead, cadmium, copper, and arsenic are below detection limits.

Total amount of poora parpam in 1000ml of sample = 1000mg

That implies 1000mg of Poora Parpam has 3.421mg of mercury
FOURIER TRANSFORM INFRARED SPECTROMETRY REPORT:

Figure 4: FTISR Raw Pooram

Figure 5: FTISR Purified Pooram
Figure 6: FTISR Poora Parpam
**TOXICITY STUDY:**
The toxicity evaluation of PooraParpam is carried in two phases.

- **Phase I** - Acute toxicity study.
- **Phase II** - Chronic toxicity study.

**ACUTE TOXICITY STUDY**

**Animals**
Wister albino rats bred in the animal house attached to the pharmacology Department, Government Siddha Medical College, Palayamkottai were used.

**Sex**
Animals of both sexes were used.

**Weight**
Animals weighing between 80-120 gm. were selected.

**Food and water**
The animals were maintained with standard animal feed and water ad-libitum.

**Number of Animals**
24 Albino rats divided into 6 groups each group consisting of 4 rats.

**Dose Levels**
The following dose levels were fixed by presuming range of least toxic to high toxic doses.

<table>
<thead>
<tr>
<th>Group</th>
<th>Dose Level</th>
</tr>
</thead>
<tbody>
<tr>
<td>I Group</td>
<td>Control</td>
</tr>
<tr>
<td>II Group</td>
<td>40 mg/100 gm body weight of the animal.</td>
</tr>
<tr>
<td>III Group</td>
<td>80 mg/100 gm body weight of the animal.</td>
</tr>
<tr>
<td>IV Group</td>
<td>160 mg/100 gm body weight of the animal.</td>
</tr>
<tr>
<td>V Group</td>
<td>320 mg/100 gm body weight of the animal.</td>
</tr>
<tr>
<td>VI Group</td>
<td>640 mg/100 gm body weight of the animal.</td>
</tr>
</tbody>
</table>
Route of administration

The drug was administered orally.

Drug preparation

The drug was weighted and taken and suspended in castor oil. The mixture was ground well before the administration. The preparation was done in such a way that 1ml of suspension contains dose ranging from 40mg to 640 mg of Poora Parpam which is given to the respective groups, as classified above in the doses level. The drug was administrated in morning and observed.

Observation

The following details were recorded

CENTRAL EFFECTS:

I. Stimulation

1. Hyperactivity
2. Pyloerection
3. Twitching
4. Rigidity
5. Irritability
6. Jumping
7. Clonic convulsions
8. Tonic convulsions

II. Depression

1. Ptosis
2. Sedation
3. Sleep
4. Loss of traction
5. Loss of pinna reflex
6. Ataxia
7. Loss of muscle tone
8. Analgesia

III. **Autonomic Effects**

1. Straub tail
2. Laboured respiration
3. Cyanosis
4. Blanching
5. Reddening
6. Abnormal secretions

At the end of 24 hours the number of animals live or dead in each group was noted and the approximate LD 50 was determined. The animals were morphologically examined for any toxic symptoms.

**CHRONIC TOXICITY STUDY:**

**Animals**

Wister albino rats bred in the animal house attached to the Pharmacology Department, Government Siddha Medical College, Palayamkottai were used.

**Sex**

Animals of both sexes were used.

**Weight**

Animals weighing between 80-120 gm. are selected.

**Food and water**

The animals were maintained with standard animal feed and water ad-libitum.
Number of Animals

12 Albino rats are divided into 3 groups each group consisting of 4 rats.

Dose Levels

Two doses were selected from the acute toxicity study. These doses did not have any acute toxicity effect and presumed to be safe for long term administration in animals.

I Group - Control

II Group - 40mg / 100 gm. body weight of the animal.

III Group - 80mg / 100 gm body weight of the animal.

Route of administration

The drug was administered orally for about 3 months.

Drug preparation

The drug was weighted and taken and suspended in Ghee, the mixture was ground well before the administration. The preparation was done in such a way that 1 ml of suspension contains dose ranging from 40 mg/ml and 80mg/ml of Poora Parpam for the groups taken. The prepared drug was administrated once a day (morning) for 90 days.

Observation

The following details were recorded before and after the drug administration.

Body weight of the animal

Haematological investigation

1. W.B.C Total count

2. W.B.C Differential count

3. Haemoglobin
Every month and at the end of the experiment, the above parameters were recorded and the results are tabulated.

One animal from each group were sacrificed at the end of the experiment and were dissected. The visceral organs like Liver, Kidney and Heart were removed from each animal and were preserved in 40% formalin solution and sent for histopathological studies.

**Histo-pathological procedure:**

The sections were stained with haemotoxillin and eosin and the histopathological report was given by Dr. Swaminathan, Professor Pathology Department, Tirunelveli Medical College.

The tabular column shown in tested parameters and changes in histopathological specimens were also documented.
Table 5: Acute Toxicity Study of Poora Parpam at control

<table>
<thead>
<tr>
<th>Observation</th>
<th>At 1 hr</th>
<th>At 2 hrs</th>
<th>At 4 hrs</th>
<th>At 24 hrs</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>I. Stimulation:</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hyperactivity</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Pyloerection</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Twitching</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Rigidity</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Irritability</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Jumping</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Clonic convulsions</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Tonic convulsions</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td><strong>II. Depression:</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ptosis</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Sedation</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Sleep</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Loss of traction</td>
<td>-</td>
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Table 8: Acute Toxicity Study at a dose of 160mg/100 gm body weight

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Table 10: Acute Toxicity Study at a dose of 640mg/100 gm body weight

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<td>-</td>
<td>-</td>
</tr>
</tbody>
</table>

--Negative + Positive
Acute Toxicity Study

The said parameters in acute toxicity study were observed on six groups (Group I, II, III, IV, V, VI). Group II, III, IV, V, VI were administrated with drugs such as 40mg, 80mg, 160mg, 320mg, 640mg /100 gm body weight of the animal respectively.

The results were tabulated in the table 1 to 6. From the table 2 to 6 it being found that the drug Poora Parpam did not produce any mortality even upto 320mg /100 gm body weight of the animal.
<table>
<thead>
<tr>
<th>S.No</th>
<th>Blood</th>
<th>At O’ day (Mean)</th>
<th>At 30th day (Mean)</th>
<th>At 90th day (Mean)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>WBC Total count</td>
<td>8900/cumm</td>
<td>9100/cumm</td>
<td>9200/cumm</td>
</tr>
<tr>
<td>2</td>
<td>Differential Count</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Neutrophil</td>
<td>28%</td>
<td>26%</td>
<td>24%</td>
</tr>
<tr>
<td></td>
<td>Eosionophil</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td></td>
<td>Basophil</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td></td>
<td>Lymphocyte</td>
<td>72%</td>
<td>74%</td>
<td>76%</td>
</tr>
<tr>
<td></td>
<td>Monocyte</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>3</td>
<td>Haemoglobin %</td>
<td>66</td>
<td>68</td>
<td>70</td>
</tr>
<tr>
<td>4</td>
<td>Body Weight</td>
<td>100 g</td>
<td>102 g</td>
<td>104 g</td>
</tr>
</tbody>
</table>

TABLE NO:8

Changes in the parameters of weight and Hematological indices

Group II animals: 40mg / 100mg body weight of the animal

<table>
<thead>
<tr>
<th>S.No</th>
<th>Blood</th>
<th>At O’ day (Mean)</th>
<th>At 30&lt;sup&gt;th&lt;/sup&gt; day (Mean)</th>
<th>At 90&lt;sup&gt;th&lt;/sup&gt; day (Mean)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>WBC Total count</td>
<td>9500/cumm</td>
<td>9700/cumm</td>
<td>9800/cumm</td>
</tr>
<tr>
<td>2</td>
<td>Differential Count</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Neutrophil</td>
<td>32%</td>
<td>28%</td>
<td>24%</td>
</tr>
<tr>
<td></td>
<td>Eosionophil</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td></td>
<td>Basophil</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td></td>
<td>Lymphocyte</td>
<td>68%</td>
<td>72%</td>
<td>76%</td>
</tr>
<tr>
<td></td>
<td>Monocyte</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>3</td>
<td>Haemoglobin %</td>
<td>68</td>
<td>70</td>
<td>72</td>
</tr>
<tr>
<td>4</td>
<td>Body Weight</td>
<td>100 g</td>
<td>105 g</td>
<td>110 g</td>
</tr>
</tbody>
</table>
TABLE NO:9

Changes in the parameters of weight and Hematological indices

Group III animals: 80mg / 100mg body weight of the animal

<table>
<thead>
<tr>
<th>S.No</th>
<th>Blood</th>
<th>At O’ day (Mean)</th>
<th>At 30th day (Mean)</th>
<th>At 90th day (Mean)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>WBC Total count</td>
<td>9200/cumm</td>
<td>9400/cumm</td>
<td>9600/cumm</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>Differential Count</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Neutrophil</td>
<td>30%</td>
<td>26%</td>
<td>20%</td>
</tr>
<tr>
<td></td>
<td>Eosionophil</td>
<td>-</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td></td>
<td>Basophil</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td></td>
<td>Lymphocyte</td>
<td>70%</td>
<td>72%</td>
<td>78%</td>
</tr>
<tr>
<td></td>
<td>Monocyte</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>3</td>
<td>Haemoglobin %</td>
<td>66</td>
<td>68</td>
<td>70</td>
</tr>
<tr>
<td>4</td>
<td>Body Weight</td>
<td>100 g</td>
<td>110 g</td>
<td>120 g</td>
</tr>
</tbody>
</table>
Table 10

Acute Toxicity Study Analysis

<table>
<thead>
<tr>
<th>Group</th>
<th>Dose in mg/100gm body weight of animal</th>
<th>No of rats</th>
<th>No of rats died</th>
</tr>
</thead>
<tbody>
<tr>
<td>II</td>
<td>40</td>
<td>4</td>
<td>-</td>
</tr>
<tr>
<td>III</td>
<td>80</td>
<td>4</td>
<td>-</td>
</tr>
<tr>
<td>IV</td>
<td>160</td>
<td>4</td>
<td>-</td>
</tr>
<tr>
<td>V</td>
<td>320</td>
<td>4</td>
<td>-</td>
</tr>
<tr>
<td>VI</td>
<td>640</td>
<td>4</td>
<td>-</td>
</tr>
</tbody>
</table>

Since there is no mortality of the animal in Acute toxicity study, lethal dose of drug need not be calculated.
Table 11

Chronic Toxicity Study Analysis

<table>
<thead>
<tr>
<th>Group</th>
<th>Dose in mg/100gm body weight of animal</th>
<th>No of rats</th>
<th>Days</th>
<th>No of rats died</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>40</td>
<td>4</td>
<td>0</td>
<td>-</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>30</td>
<td>-</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>90</td>
<td>-</td>
</tr>
<tr>
<td>II</td>
<td>80</td>
<td>4</td>
<td>0</td>
<td>-</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>30</td>
<td>-</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>90</td>
<td>-</td>
</tr>
</tbody>
</table>
Median Lethal Dose (LD 50):

It is the dose which kills half the population of the animal tested.

Since there is no mortality of the animal in chronic toxicity study, lethal dose of drug need not be calculated.

In case of Chronic Toxicity Study, with the help of physiological parameter such as haematological & Histopathological studies the drug reaction within the animal can be assessed and being tabulated respectively.
HISTO-PHATHOLOGY STUDY

HISTOPATHOLOGY OF LIVER OF RAT:

Control: Section studied shows normal liver tissue.

Low Dose Exposure: Section studied shows liver tissue with dilated central vein with congested sinusoids.

High Dose Exposure: Section studied shows liver tissue with dilated central vein with congested sinusoids.
HISTOPATHOLOGY OF KIDNEY OF RAT:

Control: Section studied shows normal kidney tissue

Low Dose Exposure: Section studied shows normal glomeruli with focal cloudy swelling of the tubules

High Dose Exposure: Section studied shows normal glomeruli with focal cloudy swelling of the tubules
HISTO-PHATHOLOGY OF HEART OF RAT:

Control: Section studied shows normal heart tissue

Low Dose Exposure: Section studied shows normal bundles of myocardial fibers.

High Dose Exposure: Section studied shows normal bundles of myocardial fibers.
DISCUSSION
DISCUSSION:

According to the research done so far, the amount of mercury in Poora Parpam is around 3.42µg/g. The therapeutic dose of Poora Parpam is usually 65mg/dose with consumption of three times a day. That shows if a person consumes Poora Parpam under these regulations, total intake in a week will be 1.2mg. Which implies total intake of mercury in a week will be 4.1µg. In 2004 the Joint FAO/WHO Expert Committee on Food Additives (JECFA) established a tolerable intake of 1.6 µg/kg bodyweight per week for methylmercury in order to protect the developing fetus from neurotoxic effects. For adults, up to about twice the tolerable intake per week would not pose any risk of neurotoxicity. So amount of mercury present in Poora Parpam is slightly (0.9µg) higher than permissible limits of mercury for a week in adults. But ingestion of 10times the dosage of drug doesn’t showed any notable toxic symptoms in animals. This contrary result in animal study may be due to the fact that the drug is administered along with castor oil as adjuvant, which may play an important role in reducing its toxic properties. Moreover, the permissible limits regulations by WHO applies mainly to long term exposure to mercury for months. But usually the drug is given only for a week.

In case of humans, some factors such as food habits may also play an important role in determining the toxicity of mercury-containing drugs. Because most of the toxicity work done by WHO is on western population, which follows very different food habits compared with a normal Indian population. For example, intake of common food ingredients such as sesame oil, turmeric, tamarind, garlic, and asafoetida may play an important role in prevention of toxic effects of mercury. This becomes more evident from the south Indian population which consumes sea food in large amount. A recent research suggest that average mercury concentration obtained in muscle of deep sea fishes that is regularly consumed by south-east Indian
population was 1.6 mg/kg dry weight (0.352 mg/kg wet weight), which is higher than the prescribed limits (0.3 mg/kg wet weight). But there are no notable toxic effects due to mercury such as Alzheimer’s disease, autism in south indian population when compared with the western population. This may be due to the protective mechanism of indian food ingredients.

In histo-pathology studies, traces of mercury are present in liver and kidney. But this may be reversible, as it didn’t produce any significant toxic symptom in animals. Usually metallothionins – a cysteine rich protein plays an important role in protection against mercury toxicity in tissues by binding with mercury. But excretion of mercury from kidney may take a long time as mercury gets deposited in glomerular tissues due to effective tubular reabsorption. However, presence of metallothionins protects liver and kidney from effective damage though it won’t play any effective role in removal of mercury from our body. Various cell culture studies have shown that turmeric, garlic and tamarind plays an important role in increasing metallothionin production in cultured cells. These data’s further supports the proposed mechanism of protective role of food diets in Indian population against mercury.

Another unexplored facet, which could affect the efficacy and toxicity of these drugs, are drug-drug interaction that occurs when they are given in combination with other herbal preparations. The fact that mercury sulfide is insoluble and does not get absorbed through blood circulation eliminates its chances of providing therapeutic benefits, since it may not react at all with the cell receptors. However, incorporation of herbal ingredients in these preparations may alter the cell uptake, distribution, and elimination profile as well as the therapeutic properties. So a detailed study on all these factors is necessary.
Summary:

This study aims at evaluating the toxicity profile of Poora Parpam, commonly used siddha drug in treatment of various metabolic disorders. Raw Pooram is first purified using piper betel and piper longum, and Poora parpam is then prepared using unique method mentioned in Aruvai maruthuvam. Basic chemical analysis was performed to study the presence of various elements present in the drug along with detailed toxicology study using animal models. According to the chemical analysis done, the amount of mercury in Poora Parpam is around 3.42µg/g. The therapeutic dose of Poora Parpam is usually 65mg/dose with consumption of three times a day. That shows if a person consumes Poora Parpam under these regulations, total intake in a week will be 1.2mg. Which implies total intake of mercury in a week will be 4.1µg. But this amount of mercury present in Poora Parpam is slightly (0.9µg) higher than permissible limits of mercury for a week in adults declared by the Joint FAO/WHO Expert Committee on Food Additives (JECFA) In 2004.

In contrary to the chemical analysis, administration of 10 times the therapeutic dosage in acute toxicity study doesn’t show any notable toxic symptoms in animals. This may be due to the fact that the drug is administered along with castor oil as adjuvant, which may play an important role in reducing its toxic properties. Moreover, the permissible limits regulations by WHO applies mainly to long term exposure to mercury for months. But usually the drug is given only for a week.

In chronic studies, Histo-pathology of kidney showed normal glomeruli with focal cloudy swelling of the tubules. But this may be reversible, as it didn’t produce any significant toxic symptom in animals. Another unexplored facet, which could affect the efficacy and toxicity of these drugs, are drug-drug interaction that occurs when they are given in combination with other herbal preparations. Although Poora
Parpam have metal contents far greater than the WHO limits, the toxicity of a preparation need not directly correlate with the metal content in the sample. The chemical nature of the metal, route of administration, dosage, residence time within the body, pharmacokinetics and dynamics, bioavailability, metabolic transformations of the preparation, age, gender, physiology, nature and stage of disease, and diet can influence the toxic manifestations of the drug. Hence a detailed study on all these factors is essential to answer the comprehensions raised by the usage of herbo-metallic drugs like Poora Parpam.

CONCLUSION
CONCLUSION:

Even though the metals are purified and believed to be non-toxic according to Siddha system, this only refers to the clinical or therapeutic dose, which is minimal. So over consumption due to improper medication/self-medication may lead to significant toxic effects. Although most of the siddha medicinal preparations have metal contents far greater than the WHO limits, the toxicity of a preparation need not directly correlate with the metal content in the sample. The chemical nature of the metal, route of administration, dosage, residence time within the body, pharmacokinetics and dynamics, bioavailability, metabolic transformations of the preparation, age, gender, physiology, nature and stage of disease, and diet can influence the toxic manifestations of the herbo-metallic preparations. Therefore, a careful analysis of all these parameters is required in order to establish the risk involved in a given herbo-metallic preparation. Most of the studies conducted thus far on mercury-based siddha medicine preparations in experimental animals have been short-term toxicity studies with use of high doses of HgS, which cannot be correlated with humans. Variations in therapeutic doses are recommended by practitioners for different ailments. Practitioners in siddha medicines adopt a holistic approach to treatment and consider the physiological aspects of an individual along with the type of disease and stage of presentation. Diet restrictions also contribute to alterations in the pharmacokinetics, and thus labeling a traditional medicine preparation as toxic based only on the metal content seems inappropriate. However, in-depth and systematic investigations are not available for these preparations. Pre-clinical studies are needed after conversion of the human therapeutic dose to an animal dose, and both short-term and long-term toxicity have to be evaluated.
Significant and substantial amount of data through these studies can provide a platform for designing human clinical trials. Even though cinnabar has been used for centuries in traditional medicine, pharmaco-vigilance never existed then and does not even prevail in the modern era. The need for patient follow-up after counseling and drug therapy was rare in earlier times, and even now it is not followed stringently. Hence, scientific evidence is lacking to confirm the safety and efficacy of these drugs. No pharmaco-therapeutic studies exist to analyze the benefits of these drugs. Shortcomings in choice of animal models and proper design of experiments to assess toxicity have hampered the risk assessment of these traditional preparations, and hence there is a requirement for more comprehensive studies to understand the ramifications of these therapeutic processes.
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13. பருக்குறி காண்டம்

14. கம்பிக்கிரி பிரார்த்திக் காண்டம் 360

15. கம்பிக்கிரி கையாம்

16. அர்ந்தீசு பார்ப்பில் 400

17. கிருமிக்குறி விபத்து மாந்தல்

18. அர்ந்தீசு கவித்து கம்பிக்கிரி காண்டம்

19. கிருமிக்குறி கையாம்

20. பருக்குறி கையாம் மலருத்துறி பிரார்த்திக் காண்டம் –சன்ன காண்டம் 600

21. கிருமிக்குறி புத்தக கையாம்