A Conceptual Study of Understanding the Effects of Phthalates on Human Health and its Management with special reference To Dooshi Visha (Cumulative Toxicity)

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ABSTRACT
Human beings are invariably accustomed to the usage of plastics. These plastics pose various health hazards on the human population. According to the Global Industry Analysts in the year 2015, 297.5 million tons of plastic were used. To increase the durability and elasticity of the plastic various plasticizers are being used. The utmost common plasticizer used is Phthalates. Phthalates are the di esters of 1, 2 – benzenedicarboxylic acid (phthalic acid). Phthalates have got various health hazards. Phthalates are nanoparticles and they surpass the placenta, breast milk, enterohepatic circulation leading to various systemic illness and complications pertaining to the same. Hence it is imperative to prevent the usage of Phthalates and also detoxification of the same has to be done based on classics. Pertaining to the classical reference it is clear that the Phthalates can be reflected to be similar with the theory of Dooshi visha (cumulative toxicity) as per Ayurveda; indulgence of the same will lead to various health hazards and complications. This paper aims to review the effect of Phthalates on human health and its management w. s. r. to Dooshi visha (cumulative toxicity). Based on the treatment notion of Dooshi Visha i.e various Panchakarma modalities one can reduce the complications as well as move towards Swasthya.

KEYWORDS
Phthalates, plasticizers, detoxification, Dooshi visha (cumulative toxicity), Nidana Parivarjana, swasthya
INTRODUCTION
Phthalates are the most commonly used plasticizers; they are a cluster of manmade chemicals termed as diesters of 1, 2-benzenedicarboxylic acid (phthalic acid). Phthalates are basically divided into high molecular weight Phthalates for e.g. di (2-ethylexyl) phthalate [DEHP], di-isononyl phthalate [DiNP], di-n-octyl phthalate [DnOP] and low molecular weight Phthalates for e.g. diethyl phthalate [DEP] and dibutyl phthalate [DBP]. High molecular weight Phthalates (Flexible vinyl) is used in the production of consumer products, food contact applications, floorboards and wall covering, and medical devices\(^1\)-\(^3\). Low molecular Phthalates are utilised in the production of personal care products, and in making polishes, as thinners and plasticizers for cellulose acetate, polishes, and coverings, including those used to provide programmed releases in some pharmaceuticals\(^3\)-\(^5\). Phthalates have a extensive range of applicability in consumer products and personal care hence has a high risk of non-occupational human exposure, which in turn causes various health hazards such as developmental anomalies, male reproductive health, female reproductive health, pregnancy outcome and respiratory health\(^6\). In Ayurveda, interpretation of Phthalates can be done under the theory of Dooshi visha (cumulative toxicity). Dooshi visha (cumulative toxicity) is a part of Sthawara, Jangama or Krutrimvisha, which cannot be banished from the body but instead becomes less persuasive after digestion or the counter action of antidotes (Prativisha) stays in the body for an extended period and vitiating it slowly\(^7\). Favorable conditions can create a variety of symptoms in a patient affected by Dooshivisha. The manifestations may be very wide from Jwara to Kushta and Unmada, hence one has to give more importance in prevention and management of Dooshi visha (cumulative toxicity)\(^8\).

OBJECTIVES
1. To collect and analyse the literature of Phthalates and human health.
2. To collect and analyse the literature review of Dooshi visha (cumulative toxicity).
3. To compare the symptoms of Dooshi visha (cumulative toxicity) with Phthalates.
4. To analyse the management principles based on the classical literature.
To fulfil the aims and objectives of this study, work has been undertaken in the following phase wise manner.
1. Conceptual study
2. Discussion
3. Conclusion
CONCEPTUAL STUDY
Phthalates and Human Health
Phthalates have an inclusive range of utility in consumer products and personal care hence non-occupational human exposure of Phthalates is high. However, route of acquaintance to Phthalates is unknown. Conventionally, ingestion has been considered an imperative route of exposure. Due to low volatility Phthalates are present in housing indoor air\textsuperscript{9-10}. Dermal contact and parenteral acquaintance from medical devices containing Phthalates may also add to exposure\textsuperscript{2-11}. On exposure, Phthalates are swiftly processed and excreted in urine and faeces\textsuperscript{1-5}. The fraction of free monoester excretion in humans differs depending on the aqueous solubility of the phthalate metabolites\textsuperscript{12-13}.

Internal Dose of Phthalates
Phthalates are extensively used in laboratory and medical products and therefore sample contamination is difficult to avoid. Human studies using the phthalate diesters as biomarkers of exposure were limited to highly exposed populations. A diverse method uses urinary phthalate monoester metabolites as biomarkers of exposure\textsuperscript{14-19}. Chromatography coupled with mass spectrometric techniques can be used to measure Phthalate monoesters in biological matrices, of which most common is high performance liquid chromatography (HPLC). Phthalate monoesters after conversion to volatile derivatives can be measured by using Gas chromatography\textsuperscript{20}.

Effects on Human Health
An assessment of data emerging from in silico, in vitro and in vivo approaches on Phthalates would provide various hazardous impacts on humans\textsuperscript{21}. The most important contrary effects of Phthalates are seen in foetal development, endocrine and reproductive anomalies, especially the so-called “phthalate syndrome”\textsuperscript{22} which are further discussed in Table-1.
These are the adverse health effects impacted by Phthalates on humans\textsuperscript{22}

> Phthalates vs. Endocrine disrupting chemicals, the EDCs
> Allergy & Asthma
> Phthalates and child health
> Phthalates and women health
> Phthalates and Men health
> Phthalates Vs Overweight and Obesity
> Phthalates Vs Cancer

Concept of Dooshi visha (cumulative toxicity)
The term Dooshivisha is a compound of two different words, ‘Dooshi’ and ‘Visha’. ‘Dooshi’ means denatured, tempered, reformed, dormant, vitiated or something which influences the system in the long run. ‘Visha’ means poison\textsuperscript{24}. Poison which is
devoid of the ten innate properties of *Visha* and unable to produce any acute symptoms of poisoning can also be termed as *Dooshivisha*. *Dooshivisha* is *Avibhavyamana* i.e the one which is not traceable due to Avarana by Kapha Dosha. Due to its ability to remain in the system for prolonged periods of time it is termed *Varshaganubandhi*.25

Table 1 Effects of Phthalates on Human health23

<table>
<thead>
<tr>
<th>Phthalate diester</th>
<th>Possible sources of exposure</th>
<th>Possible health effects</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diethyl phthalate</td>
<td>Personal-care products (e.g. fragrances), dyes, insecticides, coatings (e.g. pharmaceuticals)</td>
<td>Reduced growth rate, food consumption and increased organ weights</td>
</tr>
<tr>
<td>Di-n-butyl phthalate</td>
<td>Cellulose acetate plastics, personal care products (e.g. nail polish, cosmetics), lacquers, varnishes, coatings (e.g. pharmaceuticals)</td>
<td>Renal and hepatic effects, developmental effect and reproductive effects, cryptorchidism, reduced foetal weight, hypospadias, reduction in anogenital distance in males,</td>
</tr>
<tr>
<td>Butylbenzyl phthalate</td>
<td>Vinyl floorboards, glues and sealants, car-care merchandises, industrial solvents, toys, food wrapping, synthetic leather, personal-care products</td>
<td>Testicular toxicity, cryptorchidism, teratogenic, modulates steroid hormone levels, reduced anogenital distance</td>
</tr>
<tr>
<td>Di(2-ethylhexyl) phthalate</td>
<td>PVC plastics used in domestic products (e.g. toys, flooring and furniture, wall coverings), food wrapping, blood storage bags and medical devices</td>
<td>Hepatocellular carcinoma, testicular toxicity, teratogenic at high doses, anovulation, affects fetal growth</td>
</tr>
</tbody>
</table>

Clinical features of *Dooshivisha*26

Intoxication, fainting and discoloration, intermittent fever, oligospermia, urticaria, vomiting, epileptic attacks, increased thirst, Appearance of red patches throughout the body, indigestion, diarrhoea, insanity, distension of the abdomen, Oedema of the face and extremities, Skin disorders.

Complications of *Dooshivisha*27

Pyrexia, Diarrhea, Burning sensation, Fainting, Hiccough, Cardiac disorders, Distension of abdomen, Abdominal enlargement, Oligospermia, Insanity, Oedema, Tremors.

Transformation of *Visha* into *Dooshivisha*28

1. *Jeernam Visham* (Partly metabolized): It has got two aspects (A) When *Visha*, which is proficient of producing acute ill effects, is kept for long time, some of them may lose their original properties, ultimately getting converted into less potent *Visha*, which is *Dooshivisha*. (B) Poison (*Visha*) whether inanimate (*Sthaavara*), animate (*Jangama*) or artificial (*Kritrima*) which is not completely removed from the body or partly detoxified and being retained or amassed in the body and confined at various sites of tissues.
producing cumulative effect is Dooshivisha.

2. **Exposure to Davagni:** Exposure to heat flame or fire etc. converts Visha in to latent poison (Dooshivisha).

3. **Exposure to Vata:** Cold wind desiccates the water content of Poison (Visha) thus transforming potent Visha in to less potent Dooshivisha.

4. **Exposure to Aatapam:** Vishadravyas when exposed to sun detoxification occurs at the maximum rate, which in turn reduces the potency of poison.

5. **Naturally Less Potent (Swabhavato Gunaviprahinam):** Presence of all 10 Gunas in Visha can cause acute or sub-acute poisoning. But if anyone or more of these properties (Gunas) are absent in a particular Visha, it can become Dooshivisha that is of low potency by nature. Ingesting of these will produce symptoms of Dooshivisha which flares up in the presence of aggravating factors.

**GENERAL PRINCIPLES IN THE MANAGEMENT OF DOOSHI VISHA (CUMULATIVE TOXICITY)**

The patient of Dooshi visha (cumulative toxicity) should be administered Swedan (sudation therapy) followed by Vaman (emesis) and Virechana (purgative therapies) as discussed in Table 2, tailed by Dooshi vishari agada (antidote) for internal administration with honey.

**Table 2 Treatment principles**

<table>
<thead>
<tr>
<th>Hetu Viprit Chikitsa</th>
<th>The treatment should be opposite to the nature of causative Dosha</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vaman</td>
<td>One should take cold bath after Vamana, because poison is having hot potency and it aggravates pitta Dosha so to pacify Pitta Dosha cold water bath is indicated.</td>
</tr>
<tr>
<td>Agadapana</td>
<td>Agada (anti poisonous medicine) should be administered mixed with Honey and ghee immediately15.</td>
</tr>
<tr>
<td>Kushtaghana and Rakthashodaka Aushadha</td>
<td>For skin manifestation</td>
</tr>
<tr>
<td>Kapha Dosha Predominance</td>
<td>Vaman is indicated and application of paste of drugs (drug possess hot and penetrating property). Foods should be pungent, astringent and bitter tastes.</td>
</tr>
<tr>
<td>Pitta Dosha Predominance</td>
<td>Mild Virechana (purgations), Swedana (sudation), poultices applied very cold and foods which are bitter, astringent and sweet in taste, added with ghee.</td>
</tr>
<tr>
<td>Vata Dosha Predominance</td>
<td>Foods which is sweet, unctuous (fatty), sour, salty and added with ghee, application of drugs of the same properties and of meat as food.</td>
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**DISCUSSION**

As Phthalates are extensively used in consumer and personal care products non-occupational exposure is unavoidable, hence leads to the various health hazards. Exposure to Phthalates and its health
hazards can be understood under the notion of *Dooshi visha* (*cumulative toxicity*) based on the description in Table-3.

**Table 3 Dooshi visha** and Phthalates

<table>
<thead>
<tr>
<th>Dooshi visha (<em>cumulative toxicity</em>)</th>
<th>Phthalates</th>
</tr>
</thead>
<tbody>
<tr>
<td>Poison (<em>Visha</em>) whether inanimate (<em>Sthaavara</em>), animate (<em>Jangama</em>) or artificial (<em>Kritrima</em>) which are partially eliminated from the body or partly detoxified and being retained or collected in the body and localized at various sites of tissues producing cumulative effect is <em>Dooshivisha</em>.</td>
<td>On exposure, Phthalates are quickly metabolised and expelled in faeces and urine. Part of the Phthalates remnants in the body after phase 1 and 2biotransformation. Acquaintance to Phthalates is assessed by the rate of excretion and health hazards are based on the remnants of Phthalates in the body.</td>
</tr>
<tr>
<td><em>Kritrima Visha</em> (Artificial poison)</td>
<td>Artificial poison</td>
</tr>
<tr>
<td>Similar clinical features and complications are seen as mentioned in conceptual study</td>
<td>No specific treatment, treatment based on signs and symptoms</td>
</tr>
<tr>
<td>General principle of <em>Ayurvedic</em> management</td>
<td></td>
</tr>
</tbody>
</table>

Based on the above comparison we can clinch that Phthalates can be grouped under the notion of *Dooshi visha* (*cumulative toxicity*). As there are no specific line of treatment for Phthalates, treatment of *Dooshi visha* (*cumulative toxicity*) is applicable where the prime importance is given to *Nidana Parivarjana*.

**CONCLUSION**

The world is so vigilant about the impact of Phthalates on environment and human health. Currently it is one among the global threats. From above study, the *Lakshana* of *Dooshi visha* (*cumulative toxicity*) described in *BruhatrayiSamhita*, are near about similar to that of hazards of Phthalates exposure. The notion of *Dooshi visha* (*cumulative toxicity*) described in ancient times totally resembles in today’s lifestyle, this shows how deeply our *Aacharyas* studied about *Visha* and their properties. Based on which we can understand the effects of Phthalates on human health and its management under the notion of *Dooshi visha* (*cumulative toxicity*). Management is generally based on *Doshas* where *Shodhana* being the prime modality. It is alarming for us, to have sound knowledge of such silent poisoning, which is hazardous to our health.
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