Preservatives and their use in Ayurvedic Pharmaceutics

Abhaya Kumar Mishra¹, Aparna Sharma², K. Unnikrishna pillai³,

¹Associate Professor, ²Post Graduate Scholar, ³Professor and Head,
Dept. of PG Studies in Rasasastra and Bhaishajya Kalpana, Amrita School of Ayurveda, Kollam, Kerala

Abstract

Ayurvedic pharmaceutical history can be traced back up to Vedic period. In the initial period drugs were freshly prepared and used soon after the preparation. But as the demand for medicines increased, need of preservation of the drugs aroused. This lead to the use of natural preservatives initially, then those natural preservatives were gradually replaced by chemical preservatives. Due to increased commercialization usage of more and more chemical preservatives like benzoic acid, sodium benzoate, parabens etc. also increased. This lead to the development of several health problems in humans. Ayurveda classics have mentioned several natural methods of preservation techniques. By following the classically mentioned methods, one can avoid the irrational use of chemical preservatives by compromising the quality of the preparation.

Key word: Chemical preservatives, benzoic acid, sodium benzoate, parabens etc.
INTRODUCTION

Drug spoilage has been a problem throughout history of pharmaceutics. This lead to the introduction of the concept of preservatives. In ancient times we adopted many natural methods for the preservation of food as well as medicines. These natural products acted as preservatives as well as an ingredient in that formulation. Due to increased commercialization, the need of more potent preservatives aroused which lead to the use of more and more chemical preservatives.

PRESERVATIVES

Preservatives are the substance which is added to pharmaceutical formulations to prevent the drug spoilage by inhibiting the growth of micro-organisms or by any other means [1]. The mode of action may be inhibition of microbial growth, oxidation and certain enzymatic reactions occurring in the medicines.

Good Preservative Properties

1. Broad spectrum activity
2. Be effective over a wide pH range
3. Be inactive to the active principles of the drug
4. Not be deactivated by other ingredients
5. Be effective over the anticipated shelf period of the drug
6. Be preferably liquid and water soluble
7. Be odorless, colorless, and safe.

CLASSIFICATION

I. Natural / Class I preservatives & Artificial / Class II preservatives
II. Antimicrobials & Antioxidants

Natural / Class I preservatives

Constituents extracted from natural sources that offer intrinsic ability to protect products against microbial growth. Eg: Salt, sugar, honey etc.

Artificial / Class II preservatives

These are group of synthetic chemical substances. Examples are nitrates, sulfites, benzoates, potassium sorbate etc.

Antimicrobials:

These preservatives inhibit the growth of bacteria, yeasts, molds or fungi by creating an environment hostile to them. Examples are nitrates, nitrites etc.

General Mode of Action of Antimicrobial Preservatives

The effects of these antimicrobial preservatives are on the microbial cellular targets. But it is difficult to assign a precise target for a specific class of preservative because the preservative capacity does change with concentration. These antimicrobial preservatives can often interfere with several different microbial cellular mechanisms. Also causes oxidation of cell wall constituents which all lead to cell death. These antimicrobial preservatives provide limited protection against viral contamination.

Table No. 1: Site of action of different Antimicrobial preservative groups.

<table>
<thead>
<tr>
<th>CELL WALL</th>
<th>CYTOPLASMIC MEMBRANE</th>
<th>CYTOPLASM</th>
</tr>
</thead>
<tbody>
<tr>
<td>Phenol</td>
<td>2-phenoxy ethanol</td>
<td>2-phenoxy ethanol</td>
</tr>
<tr>
<td>Aryl and alkyl acids</td>
<td>Parabens</td>
<td>Aryl and alkyl acids</td>
</tr>
<tr>
<td>Organo mercurial</td>
<td>Organo mercurial</td>
<td>Chlorhexidine</td>
</tr>
<tr>
<td>EDTA</td>
<td>EDTA</td>
<td>Formaldehyde donors</td>
</tr>
<tr>
<td>Chlorohexidine</td>
<td>Chlorohexidine</td>
<td>Halogenated preservatives</td>
</tr>
<tr>
<td>Glutaraldehyde</td>
<td>Formaldehyde donors</td>
<td></td>
</tr>
<tr>
<td>Anionic surfactants</td>
<td>Benzalkonium chloride</td>
<td></td>
</tr>
</tbody>
</table>

Antioxidants

Oxidation is one among the major causes of drug spoilage. Antioxidant preservatives prevent the oxidation of active substances and excipients in the finished product. Examples are BHT, ascorbic acid, sodium edetate etc.

Influence of Product pH

In extreme acidic and alkaline solution, most bacterial growth is significantly retarded, which reduces the need of preservative. For example bacterial growth is absent in suktha kalpana which is highly acidic and kshara kalpana which is highly alkaline in nature. In general, microbial growth is optimal between pH 6 – 8.

E-Number

E numbers are uniform codes for substances that can be used as food additives for use within the European Union and Switzerland. In 1964, preservatives were added in the list of E-numbers.
**Preservatives in Ayurvedic Pharmaceutics**

*Parabens*

Parabens are a class of widely used preservatives in cosmetic and pharmaceutical products. These are chemically a series of para hydroxybenzoates or esters of para hydroxybenzoic acid. These compounds, and their salts, are used primarily for their bactericidal and fungicidal properties.

1. **Butyl paraben**
   It is an organic compound with the formula C_{11}H_{15}O_3. Butyl paraben is proven to be a highly successful antimicrobial preservative in cosmetics. This acts as both bactericidal as well as fungicidal preservative. The popularity is due to its effective antimicrobial properties, in particular those against mold and yeast.

2. **Ethyl paraben**
   Its chemical formula is C_{6}H_{13}O_3. This preservative is used as an antifungal agent. Its E number is E214. If used in excess it may cause skin irritation, contact dermatitis and rosacea [iii]. On the skin may react with UVB leading to increased skin ageing and DNA damage. Ethyl paraben act as xenoestrogen.

3. **Methyl paraben**
   Its chemical formula is C_{6}H_{12}O_3. It is the methyl ester of p-hydroxybenzoic acid. This act as an anti-fungal agent. Methyl paraben is considered generally recognized as safe (GRAS) for food and cosmetic antibacterial preservation. Maximum permitted level is 0.4%. This gets readily absorbed from the gastrointestinal tract or through the skin. It is hydrolyzed to p-hydroxybenzoic acid and rapidly excreted in urine without accumulating in the body.

**Benzoic Acid**

Chemical formula of benzoic acid is C_{6}H_{5}COOH. This is a colorless crystalline solid and a simple aromatic carboxylic acid. E-Number of benzoic acid is E210. Its maximum permitted level is 0.1%. This inhibits the growth of mold, yeast and some bacterial species.

**Sodium benzoate**

Chemical formula of sodium benzoate is C_{6}H_{5}COONa or C_{6}H_{4}NaO_2. It is the sodium salt of benzoic acid. E-Number of sodium benzoate is E211. Maximum permitted level is 0.1%. One gram of sodium benzoate is soluble in 2 ml of water, 75 ml of ethyl alcohol and 50 ml of 90 % ethyl alcohol [iv]. Sodium benzoate is safe for consumption within the range 647-825 mg / kg of body weight /day. This is used as an antimicrobial agent in medicines which naturally are in the pH range below 4.5.

**Metabolism**

Sodium benzoate which we intake get transported to liver. Within mitochondria of hepatocytes it combine with coenzyme A to form benzyol coenzyme A. Benzoyl coenzyme A combine with glycine to form hippuric acid. Hippuric acid is finally excreted through urine. Average excretion is about 0.7g/day.

**Side effects**

Research work published in 2007 for the UK’s Food Standards Agency (FSA) suggests that certain artificial colors, when paired with sodium benzoate, may be linked to hyperactive behavior. Ascorbic acid (vitamin C) when used along with sodium benzoate, we get benzene, which is a known carcinogen [iv]. In some persons sodium benzoate may produce nausea and vomiting. Because of structural similarities between benzoate and salicylates, exacerbation of peptic ulcer, mild hyperventilation, and mild respiratory alkalosis may develop. Hypernatremia is possible, especially in patients with diminished renal function [v].

**Present Scenario**

In the present state the type and concentration of preservatives used by major pharmacies lack uniformity. In almost all Ayurvedic pharmaceutics, a mixture of 2-3 class 2 preservatives are used which is restricted by Prevention of Food Adulteration Act 1954. Even in Āsavārīṣṭas, some pharmacies are adding preservatives which is not at all needed. From different studies it was found that the level of preservatives added was even 8-10 times higher than the level permitted. So more researches must be done to keep the preparation stable with lesser amount of preservatives.

**Conclusion**

In Ayurvedic Classics Āsavārīṣṭa or shelf life for each preparation is mentioned in detail. In Āsavārīṣṭa Ayurveda there is no need of preservatives at all since the self-generated alcohol itself acts as a preservative. If we look for proper pāka and siddha lakshana in Avaleha, Ghrita and Taila, these preparations can be stored up to the duration which is mentioned in classics. By following the classically mentioned methods, one can avoid the irrational use of chemical preservatives by compromising the quality of the preparation.
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CORRESPONDING AUTHOR

Dr. ABHAYA KUMAR MISHRA MD (AYU), PhD
Associate Professor, Dept. of Rasashastra & Bhaishajya Clappana, Amrita School of Ayurveda,
Kollam – 690525, Kerala
E-mail: drabhayamishra08@gmail.com

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