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A Succinct Characterization and Comparison of Xylene and its Substitutes - Review

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Abstract: ***Xylene, an aromatic hydrocarbon is the most routinely used clearing agent during tissue processing but it is considered to be hazardous. The ill effects of xylene have been discussed long ago and few studies have been done in the recent past to introduce a safer alternative of xylene without compromising the quality. Therefore, the present review aims to briefly describe the xylene and its noxious effects and other safer compounds which may be an alternative to xylene.***

Keywords: Xylene, Substitues, Methyl salicylate, Kerosene, Ultraclear, SBO

1. Introduction

Xylene is an aromatic hydrocarbon, a basic element of wood, petroleum and coal tar and chemically an admixture of two methyl groups attached to a benzene ring.[1,2] It is a achromatic, sweet-smelling compound available in both liquid and gas form.[3]

In histopathology, xylene is routinely used clearing agent in tissue processing.[4] The trade names of xylene are xylol, dimethyl benzene, mixed xylene and violet 3. It is a constituent of BTX (Benzene, Toulene, and Xylene) aromatic hydrocarbons extracted from "Reformate", a gasoline blending stock produced by catalytic reforming.[5]

Ruinous Effects of Xylene

Xylene is a noxious chemical and its long term exposure is slanderous to health.[3] It releases a vapor that upon inhalation, ingestion or contact causes CNS depression, dizziness, GI effects such as nausea, vomiting, loss of appetite, respiratory depression, skin erythema, scaling, and irritation. Heart and kidney injuries have also been reported.[6,7]

Xylene upon ingestion gets primarily metabolized in liver by oxidation of a methyl group and conjugation with glycine to produce methyl hippuric acid which is excreted in the urine. The effects of xylene on tissues are due to the enfeeblement of ATP in the injured cells.[4,5,6.7]

Substitutes to Xylene

Methyl salicylate

Methyl salicylate or wintergreen oil is a yellow or reddish colored liquid with a distinctive aroma.[8,9] It is an organic ester obtained from the esterification of salicylic acid with methanol. It has a refractive index of 1.535-1.538 and its clearing effect are a result of the high refractive index, which equates with that of the cell wall.[9,10,11]It is three times pricey than xylene but nearly 40% less than that of cedarwood oil.[8]

It is also used as a rubefacient in deep heating liniments, in the fragrance industry and as a flavoring agent in candy.[9]

Kerosene

It is a flammable hydrocarbon liquid, the name derived from Greek – Keros- wax. It is a thin, clear liquid obtained from fractional distillation of petroleum between 150° C and 275°C.[3.4,] It is contemplated as non-carcinogenic and non-teratogenic. The acute effects in administating of kerosene are minimal if used under current safety practices.[12] Chronic exposure can cause dermatitis in laboratory personnel.[4]

In the histopathology laboratories as a clearing agent, increasing the clearing time than that of xylene in tissue processing, improves the quality of sectioning and staining. Kerosene showed better nuclear and cytoplasmic morphology, clarity, uniformity, and crispness of staining when compared to xylene. [12,13]

Kerosene is mainly used as a cooking fuel, to prevent mosquitoes breeding in pools, as a solvent and reaming lubricant.[4]

Ultraclear™

It is a colorless, odorless isoparaffin based liquid that contains C11-12 hydrocarbons that are derived from crude oil fractionation. It is ecologically innocuous and exhibits no toxic effects on humans.[3,14] Tissue cleared with ultraclear™ are easy to cut and produced good results for H&E and IHC methods. It is less toxic, less flammable, and easier to handle than xylene, but it is costly.[3]

SBO

It is a non-toxic, colorless, odorless mixture of white oil and N-heptane. It is obtained by hydrogenation of white oil through the addition of hydrogen atoms to alkenes. Hydrogenation reduced desultory hence improved safety properties but still remains compatible with alcohol and paraffin as required for tissue clearing.[2,14]

Tissue processed with SBO showed no cellular shrinkage and retains valuable diagnostic information. The tissue can be used in various diagnostic procedures including H&E stains, special stains, IHC etc. Kunhua et al, found the results in IHC staining were comparable or superior to xylene so it may be a promising substitute to xylene.[2]

Table 1: Composition Of Xylene (Commercial)

Component	Percentage
m-Xylene	40-65%
p-Xylene	20%
o-Xylene	20%
Ethyl benzene	6-20%
Toulene	Traces
Trimethyl benzene	Traces
Phenol	Traces
Thiophene	Traces
Pyridine	Traces
Hydrogen sulphide	Traces

Table 2: Properties of Xylene, Methyl Salicylate, Kerosene, Ultraclear^{tm} And Sbo

Entity	Appearance	Odor	Molecular weight	Melting point	Boiling point	Flash point
o-Xylene	Colorless liquid	Sweet smell	106.17 gm/mol	-24°C	144.4°C	32°C
m-Xylene	Colorless liquid	Sweet smell	106.17 gm/mol	-48°C	139°C	27°C
p-Xylene	Colorless liquid	Sweet smell	106.17 gm/mol	-13.2°C	138.35°C	27°C
Methyl salicylate	Colorless liquid/ Yellow to red	Wintergreen odor	152.15 gm/mol	-8.6°C	220-224°C	96°C
Kerosene	Colorless	Pungent	170 gm/mol	-48°C	170-325°C	37-65°C
Ultraclear^{TM}	Colorless	Odorless	Not determined	Not determined	173-193°C	56°C
SBO	Colorless	Odorless	256gm/mol		250° C	196°C

2. Conclusion

In laboratories, the utilization of xylene is in jeopardy due to its occupational risk to the histotechnicians. Latterly, few studies using other compounds as clearing agent have been done as they seek to oust the xylene but without conciliating the staining quality. The present review discussed and compared the four safer alternatives namely methyl salicylate, Kerosene. Ultraclear^{TM} and SBO to xylene but extensive research in large tissue samples using various diagnostic procedures need to be carried out.

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