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ORIGINAL ARTICLE

Access this article online

Website: www.ijrh.org

DOI: 10.4103/0974-7168.135642

Quick Response Code:

Leaching of plastic polymers by plastic vials used for storing homoeopathic medicines: A preliminary study

Neeraj Gupta[1], R. K. Saxena[1], B. Sharma[2], S. Sharma[2], A. K. Agrawal[2], M. Jassal[2], Raj K. Manchanda[3]

[1]Department of Organon of Medicine, Nehru Homoeopathic Medical College and Hospital, New Delhi, [2]Department of Textile Technology, Indian Institute of Technology, New Delhi, [3]Central Council for Research in Homoeopathy, Janakpuri, New Delhi, India

Address for correspondence:
Dr. Neeraj Gupta,
Reader (NFSG), Department of Organon of Medicine, Nehru Homoeopathic Medical College, Defence Colony, New Delhi - 110024
E-mail: drneerajgupta2003@yahoo.co.in.

Received: 10-06-2014
Accepted: 10-06-2014

ABSTRACT

Background: In Homoeopathy, plastic containers/vials are used for the storing/dispensing of ethanol-based medicines instead of glass. Various studies have suggested that plastic components that leach out in stored substances tend to cause contamination and may produce adverse effects in living systems. The present study was aimed to find out chemical composition and leaching behaviour of commonly used plastic vials (PVs) if any during the storage of ethanol-based homoeopathic medicines in optimal environment.

Material and Methods: The experiments were conducted on two sample sets of PVs. Chemical properties of PV were assessed by Fourier Transform Infrared Attenuated Total Reflectance (FTIR-ATR) spectroscopy. PV were cut separately [sample-1 (S-1) and sample-2 (S-2)] and immersed in Homoeopathic Grade Ethanol (HGE) in conical flask and stored for 7 days at ambient temperature (25° ± 5C) with constant rotary shaking. After 7 days, S-1 and S-2 of PV in Homoeopathic Grade Ethanol (HGE) were decanted and filtered. Aliquots (A1 and A2) were analysed by proton nuclear magnetic resonance spectroscopy (H^1 NMR). The spectral graph obtained by FTIR-ATR spectroscopy for PV compositions and spectral graph obtained by H^1 NMR spectroscopy for PV ethanol aliquots were examined for PVs material and PV leaching effect in HGE.

Results: FTIR-ATR spectra showed that PV are made up of two types of polyolefin's compounds i.e. Low Density Polyethylene (LDPE) and Linear Low Density Polyethylene (LLDPE). Aliquots of PV in HGE showed the presence benzophenone and its methyl derivative, heat and light stabiliser (2, 2, 6, 6-tetramethylpiperidine and amino derivative), antioxidant (4, 4'-thiobis and 2-tertbutyl-5-methylphenol) and plasticizer bis 2-Diethylhexyl phthalate (DEHP) or Dioctyl phthalate (DOP). Results of study suggest that PVs leach out plastic polymers in HGE.

Conclusion: This preliminary experiment suggests that it is not safe to use LDPE/LLDPE plastic for storing/dispensing ethanol based homoeopathic medicines. Further study with other grades of plastic is desirable.

Keywords: FTIR-ATR and, (H^1 NMR) spectroscopy, Homoeopathic grade ethanol, Leaching, LDPE, LLDPE, Plastic vials, Polymers, Storage

INTRODUCTION

Plastic products of different quality are used for storing and dispensing of homoeopathic medicines instead of glass which is recommended in the classical texts.[1] Several studies found that plastic polymers leach out in stored liquids (water, milk, beverages, etc.) and might cause adverse effects in living beings.[2-5] Several research studies based on plastics suggest that released or migrated plastic compounds in surrounding are toxic and harmful to human health, in many direct or indirect ways.[6-9] Phthalates or esters of Phthalic acid are commonly used as plasticisers (substances added to plastics to increase their flexibility.[10,11] Di 2-ethylhexyl phthalate, dibutyl phthalate, di-isononylphthalate, di-isodecyl phthalate, benzyl-butyl-phthalate, dioctyl phthalate and di-n-octyl- phthalate are few phthalates generally used in converting polyvinyl chloride from a hard plastic to a flexible plastic.[10,11] Mother tinctures in Homoeopathy are generally made from animal, plants and metallic compounds and use high purity ethanol because of its excellent solvent properties, inertness and non-toxic nature. There is a possibility that plastic substances may leach out and contaminate homoeopathic medicines stored/ dispensed in plastic containers/vials. Several types of plastics are used such as Low Density Polyethylene, Linear Low Density Polyethylene, High Density Polyethylene. A sophisticated preliminary chemical study has been done to study the leaching properties of commonly used homoeopathic plastic vials (PVs) of LDPE and LLDPE available in the open market and migration of plastic polymers in Homoeopathic Grade Ethanol (HGE) in acute exposure, if any.

MATERIAL AND METHODS

Material

Different kinds of homoeopathic PVs were procured randomly from local vendors/suppliers of homoeopathic materials. Diluent HGE (90%) was obtained from certified homoeopathic dispensing/ manufacturing firm from Delhi for present study.

Methodology

1. Identification of chemical composition of different PVs

PVs procured from local markets were subjected for Fourier Transform Infrared Attenuated Total Reflectance (FTIR-ATR) analysis to identify the chemical composition of plastic material used for manufacturing of vials. It is found that these vials can be distinguished into two categories i.e. having two different chemical compositions of polyolefin's compounds i.e. Low-Density Polyethylene (LDPE) and Linear Low-Density Polyethylene (LLDPE). These vials were separated and coded as S-1 (LDPE) and S-2 (LLDPE) according to their chemical composition for further study. A typical spectral graph obtained for LDPE PVs by FTIR-ATR is shown in Figure 1.

2. Preparation of S-1 (LDPE) and S-2 (LLDPE) in HGE

PVs i.e. S-1 (LDPE) and S-2 (LLDPE) were cut into small pieces and immersed into homoeopathic grade ethanol (HGE) to investigate its leaching behavior at 25 ± 5°C ambient temperature for 7 days. S-1 (LDPE) and S-2 (LLDPE) were taken by 3.4 wt. % and 6.2 wt. % of total volume of HGE, respectively, as shown in Figure 2 in conical flasks. After 7 days, the HGE from both the samples were decanted separately and evaporated at the 65°C by using Rotary Evaporator to yield

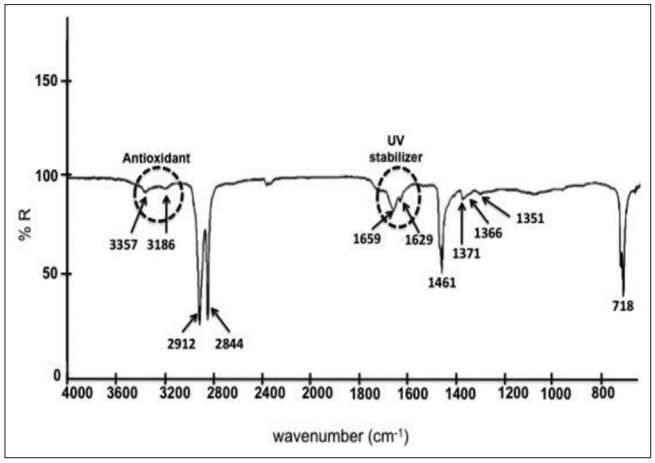

Figure 1: Fourier Transform Infrared Attenuated Total Reflectance (FTIR-ATR) of sample 1 (low-density polyethylene, LDPE) PVs

Figure 2: Sample 1 and Sample 2 in homoeopathic grade ethanol at 25 ± 5°C

their residues. Both the residues of S-1 (LDPE) and S-2 (LLDPE) were analysed by H^1 proton NMR to elucidate their chemical constituents after leaching.

3. Characterisation of residues of S-1 (LDPE) and S-2 (LLDPE) by $^1H_1$-NMR spectroscopy

Leached out residues of LDPE (S-1) and LLDPE (S-2) PVs were analysed by proton NMR spectroscopy. For every analysis with H^1 NMR, the instrument was calibrated with $CDCl_3\delta$ (ppm) and showed the chemical shift values at 0.00 and 7.19 ppm reference peak for TMS and deutrated chloroform solvent, respectively. In H^1 NMR spectral graph analysis of S-1 and S-2 residues, it was found a chemical shifts at 7.47, 7.65 ppm and assigned for benzophenone, which is used as ultraviolet (UV) stabiliser. While 4-amino-2, 2, 6, 6-tetra methylpiperidine is used as heat and light stabilisers gives characteristic peaks at 0.84, 1.08, 1.12, 1.18 and 1.79, 3.07 ppm. An anti-oxident named as 4,4´-thiobis (2-tert-butyl-5-methylphenol) is also present in residue, which gave peaks at 1.28, 2.26, 4.61-4.94, 6.92, 7.01 ppm. On the other hand, the chemical shift values at 0.90-0.92 and 1.27-1.63 and 4.21 ppm correspond to plasticiser Di Octyl Phthalate (DOP). The peaks from 0.90-1.63 ppm overlay with the peaks of 4-amino-2, 2, 6, 6-tetra methylpiperidine and result in high intensity peaks in this range. Besides, numerous small and medium intense NMR peaks exist due to unidentified impurities of sample [Figure 3].

RESULTS

The results suggest that PVs used for storing and dispensing homoeopathic medicines leach out different plastic components and additive compounds. HGE procured from supplier was analysed with proton NMR spectroscopy to confirm its purity as it was used as solvent in present study. Spectral graph obtained by H^1 NMR spectroscopy of homoeopathic grade ethanol showed definite chemical shift values for ethanol at 1.1 ppm level, i.e. (triplet, CH_3), 2.4 ppm (singlet, OH) and 3.6 ppm (quadrate, CH_2), which indicates that ethanol used in the present study contains no impurities [Figure 4].

Preliminary leaching investigation studied the migration of plastic polymers in stored HGE in commonly used PVs for dispensing medicines. Composition of PVs and leached substances in aliquots was analysed by FTIR-ATR and H^1 NMR spectroscopic techniques. PVs used for dispensing of homoeopathic medicines have been found to be composed of two types of plastic materials LDPE and LLDPE polymers in FTIR-ATR analyser. Whereas, results of stored homoeopathic grade ethanol aliquots (after 7 days) of two types of PVs showed the presence of UV stabilisers (Benzophenone's), heat and light stabilisers (methylpiperidine's), antioxidants (methylphenols) and plasticiser (Dioctyl phthalate's) contents when studied by H^1 NMR chemical analyser. Results of our short term study (7 days) found leaching of plastic polymers compounds from homoeopathic dispensing PVs in the surrounding in HGE [Table 1]. Several research

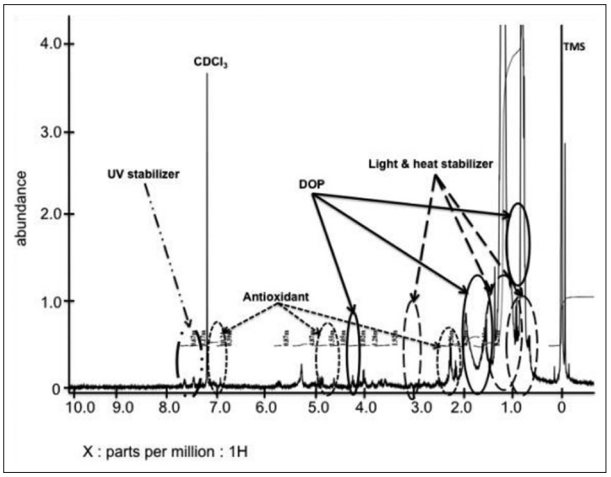

Figure 3: Proton nuclear magnetic resonance (NMR) of residue of Sample 1 (low density polyethylene, LDPE)

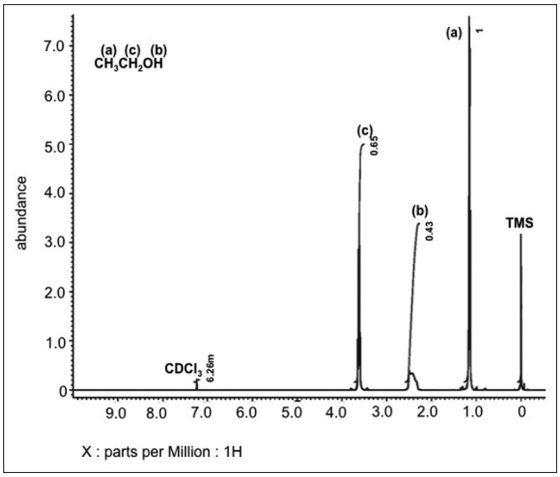

Figure 4: H^1 nuclear magnetic resonance (NMR) of homoeopathic grade ethanol spectral graph

Table 1: Plastic compounds leached out from plastic vials S-1 and S-2 in homoeopathic grade ethanol after 7 days

Name of compound leached	Sample-1	Sample-2
Ultraviolet (UV) stabilisers	(low-density polyethylene, LDPE) Benzophenone	(linear low-density polyethylene, LLDPE) 4-methylbenzophenone
Heat and light stabilisers	4-amino-2,2,6,6-tetra methylpiperidine	2,2,6,6-tetramethylpiperidine
Antioxidants	4,4′-thiobis (2-tert-butyl-5-methylphenol)	4,4′-thiobis (2-tert-butyl-5-methylphenol)
Plasticiser	Dioctyl phthalate (DOP)	Dioctyl phthalate (DOP)

studies found adverse effects of leached out plastic polymers in living beings after prolonged use.[12-14]

DISCUSSION

In the present preliminary study, leaching/migration of chemical contents in stored rectified ethanol homoeopathic PVs were investigated. Leached substances were analysed and illustrated by modern advanced FTIR-ATR and proton NMR spectroscopic techniques.

Homoeopathic PVs were procured from different local sources, its plastic characteristics were analysed by FTIR-ATR spectroscopy, to ascertain the type of plastic materials used in its development/ manufacturing. It was found that vials are made from two types of plastic polymers, having two different chemical compositions of polyolefin's compounds i.e. Low-Density Polyethylene (LDPE) and LLDPE. According to the chemical composition of PVs coded as Samples 1 (LDPE) and Sample 2 (LLDPE) for the study.

Homoeopathic grade rectified ethanol (90% by volume) was acquired from certified local homoeopathic dispenser/manufacturer and was used for the study. Chemical composition of rectified ethanol was analysed by proton NMR spectroscopy to assess and identify the purity of rectified ethanol. It is most important to mention that rectified ethanol used should not contain any impurity, so that the results are not altered due to ethanol adulteration. It is observed in rectified alcohol spectra graph that H^1 NMR ($CDCl_3$) δ (ppm) showed no chemical shift at 0.00 and 7.24 ppm, to corresponding reference peak for TMS (Trimethylsilane) and deutrated chloroform ($CDCL_3$) solvent. The chemical shift values are found at 1.1 ppm (triplet, CH_3), 2.4 ppm (singlet, OH) and 3.6 ppm (quadrate, CH_2). Rectified ethanol spectra showed that rectified ethanol which is used in present study as solvent has 100% purity and no other peaks were observed in rectified ethanol spectra graph due to impurities.

CONCLUSION AND RECOMMENDATION

This experiment has shown that commonly used PVs in homoeopathic practice were composed of LDPE and LLDPE polymers. It reflects that plastic chemicals leach out and contaminate homoeopathic medicines even at 25°C ambient temperature within 1-week period. Hence, it is recommended that PVs of LDPE, LLDPE should not be used for storing and dispensing homoeopathic medicines. Further studies with more stable plastic such as HDPE (Grade 4) are desirable.

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How to cite this article: Gupta N, Saxena RK, Sharma B, Sharma S, Agrawal AK, Jassal M, *et al*. Leaching of plastic polymers by plastic vials used for storing homoeopathic medicines: A preliminary study. Indian J Res Homoeopathy 2014;8:95-9.

Source of Support: Nil, **Conflict of Interest:** None declared.

होम्योपैथिक दवाइयों के भंडारण के लिए प्रयुक्त प्लास्टिक शीशियों द्वारा प्लास्टिक पॉलीमर (बहुलक) का निक्षालन (लीचिंग): एक अध्ययन

पृष्ठभूमि: होम्योपैथी में, एथेनोल आधारित दवाइयों को रखने/वितरित करने के लिए कांच के स्थान पर प्लास्टिक के पात्र/वायल का प्रयोग किया जाता है। कई अध्ययनों से पता चला है कि प्लास्टिक पदार्थों का भंडारित पदार्थो में होने से संदूषण हो सकता है और जीवित तंत्रों में दुष्प्रभाव उत्पन्न हो सकते हैं। वर्तमान अध्ययन का उद्देश्य सामान्य वातावरण में एथेनाल आधारित होम्योपैथिक दवाओं के भंडारण के लिए सामान्य रूप से प्रयुक्त प्लास्टिक वायल के रासायनिक संगठन और निक्षालन व्यवहार का पता लगाना था।

विधियां: प्लास्टिक वायल (पीवी) के दो नमूना सेट पर प्रयोग किए गए। पीवी के रासायनिक गुणों की समीक्षा फूरियर ट्रांसफोर्म इन्फ्रा रेड एटेनुएटेड टोटल रेफ्लेक्टेंस (एफटीआईआर–एटीआर) स्पेक्ट्रोस्कोपी द्वारा की गयी। प्लास्टिक वायलों को अलग–अलग काटा गया ,नमूना–1 (एस–1) और नमूना–2 (एस–2), और होम्योपैथिक ग्रेड एथेनोल से भरे शंक्वाकार फ्लास्क में सहिष्णु तापमान (250 डिग्री ^{c} 5) पर सात दिनों के लिए रखा गया जिसे लगातार घुमाते हुए हिलाया गया। सात दिनों के बाद, होम्योपैथिक एथेनाल में पीवी के एस–1 और एस–2 को निस्तारण करके छाना गया। प्रोटोन न्यूक्लियर मैग्नेटिक रेसोनेंस स्पेक्ट्रोस्कोपी (एच1 एनएमआर) द्वारा एलिकोट्स का विश्लेषण किया गया। पीवी संगठन के लिए एफटीआईआर–एटीआर स्पेक्ट्रोस्कोपी द्वारा प्राप्त स्पेक्ट्रल ग्राफ और पीवी एथेनाल एलिकोट्स के लिए एच1 एनएमआर स्पेक्ट्रोस्कोपी द्वारा प्राप्त स्पेक्ट्रल ग्राफ की प्लास्टिक वायल सामग्री और एचई में पीवी निक्षालन प्रभाव के लिए जांच की गयी।

परिणाम: एफटीआईआर–एटीआर स्पेक्ट्रा द्वारा प्रदर्शित हुआ कि पीवी दो प्रकार के पोलीफीन यौगिकों द्वारा बने होते हैं, निम्न घनत्व पोलीएथिलीन (एलडीपीई) और रेखीय निम्न घनत्वीय पोलीएथिलीन (एलएलडीपीई)। एचई में पीवी के एलिकोट्स में बेन्जोफीनोन और इसके मैथिल व्युत्पन्न, ऊष्मा और प्रकाश स्थिरक (2,2,6,6–टेट्रामैथिल पाइपरआईडीन और एमिनो व्युत्पन्न), अनाक्सीकारक (4,4'– थिओबिस और 2–टेट्रा ब्युटिल –5–मैथिल फिनॉल) और प्लास्टीकारक (बिस 2–डाईएथिलहेक्सिल थैलेट (डीईएचपी) या डाईओक्टिल थैलेट (डीओपी) की उपस्थिति प्रदर्शित हुई। अध्ययन के परिणाम से पता चला कि एचजीई में प्लास्टिक वायल प्लास्टिक पॉलीमर (बहुलक) निक्षालन करते हैं।

निष्कर्ष: प्रारंभिक प्रयोग से पता चलता है कि एथेनाल आधारित होम्योपैथिक दवाओं के भंडारण/वितरण के लिए एलडीपीई/एलएलडीपीई प्लास्टिक सुरक्षित नहीं है। प्लास्टिक के अन्य ग्रेड के साथ अध्ययन वांछनीय है।

मुख्य शब्द: एफटीआईआर–एटीआर और एच1दृएनएमआर स्पेक्ट्रोस्कोपी, होम्योपैथिक ग्रेडएथेनाल,निक्षालन(लीचिंग),एलडीपीई/एलएलडीपीई,प्लास्टिक शीशी, बहुलक, भंडारण