HUMAN RISK ASSESSMENT: TOXICITY ISSUES AND CHALLENGES ASSOCIATED WITH MIXTURE OF CHEMICALS RELEASED DURING PLASTIC REUSE AND RECYCLING

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Introduction

BPA is used in polycarbonate plastic and epoxy resins, plastic consumer products like toys, water pipes, food container, infant feeding bottles and other products.

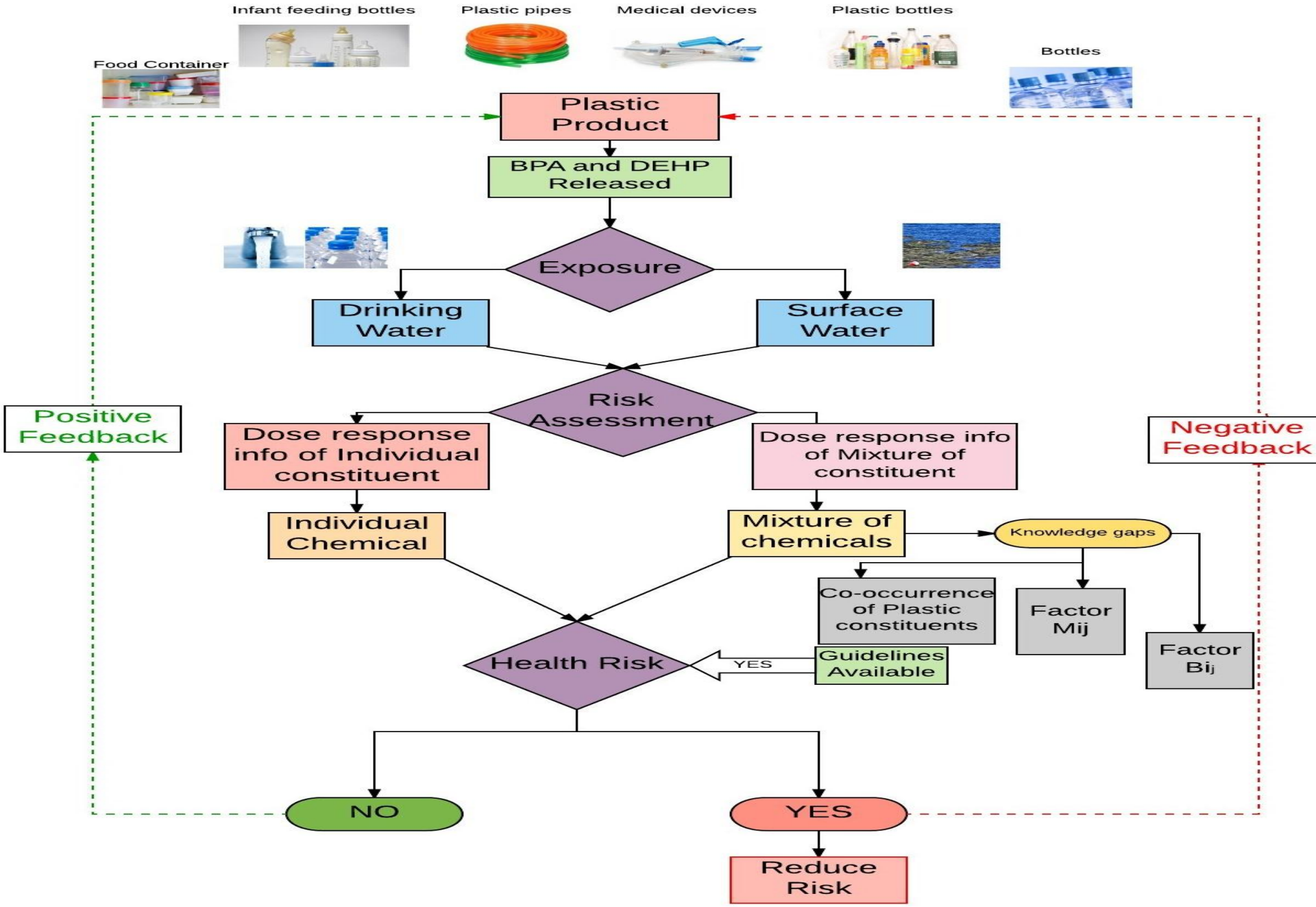
DEHP is used as plasticizer found in toys, building material, water bottles, flooring, and medical products.

Comprehensive risk assessment for simultaneous exposure of two or more than two plastic based EDC (Endocrine disrupting chemicals) have been not yet done.

Objective

Understand various gaps in literature to conduct risk assessment from exposure of human to mixture of BPA and DEHP.

Identification of risk associated with interacting effect of these plastic constituents on human, could help in suggesting actions to address knowledge gaps.



SCHEMATIC SHOWING RISK ASSESSMENT PROCESS

Methodology

Scenario

- Plastic products releases plastic constituents like BPA and DEHP into environment—land, water and air.
- Human are exposed to these constituents through different routes:
- Drinking Water
- Surface water

Hazard Identification

- Toxicity of constituents depends on physical, chemical ,and toxicokinetics properties.
- BPA exposure has shown many adverse outcomes to children and adults including reproductive and developmental effects.
- DEHP has adverse effect on liver, reproductive tract, kidney and lungs .

Exposure Assessment

- Average daily dose:

$$\mathrm{ADD} = \frac{\mathrm{C_d} \times \mathrm{DI_d}}{\mathrm{BW}} \qquad 1a$$

C_d: Contaminant level in drinking water(ng/L)

DI_d: Average daily intake of drinking water (L/d)

BW: Body weight (kg)

$$ADD = \frac{C_s \times DI_s}{BW} \qquad 1b$$

Cs: contaminant level in drinking water (ng/L)

DIs: Average daily intake while swimming in surface water (L/d)

BW: Body weight (kg)

Body weight	DI_d(Drinking water)	DI_s (Swimming)
60Kg	2L/d	0.1L/D

Dose- Response

- RfD value for mixture of DEHP and BPA not available.
- Some of the studies suggest BPA and phthalates, can promote epigenetic transgenerational inheritance of adult onset disease (Manikkam et al.,2013).
- RfD value for individual chemical as shown in table(US EPA)

Plastic constituent	RfD (mg/kg/day)	PF (/mg/kg/day)
BPA	5×10^{-2}	-
DEHP	2×10^{-2}	1.4×10^{-2}

Risk Characterization

- Risk Estimate Individual Chemical

- Individual Chemical—Non-Cancerous effect

$$\mathrm{HQ(Hazard\ Quotient)} = \frac{\mathrm{ADD}}{\mathrm{RfD}} \qquad 2$$

Individual Chemical—Cancerous effect

Incremental life time risk

$$LCR = CDI \times PF \quad (3)$$

$$CDI = \frac{C \times CR \times EF \times ED}{BW \times AT} \quad (4)$$

CDI is chronic daily intake by ingestion (mg/kg day), CW is chemical concentration in water (mg/L), IR is ingestion rate (L/day), EF is exposure frequency (days/year), ED is exposure duration (years), BW is body weight (kg), AT is averaging time.PF is Potency Factor.

HQ<1 (No risk)

HQ>1 (Potential risk)

- **Risk Estimate for Mixture of Chemicals**
- When there is no interaction—Dose additivity

$$HI = \sum_{j=1}^{n} HQj \qquad 5$$

- When there is interaction between Chemicals

$$\mathbf{HIint} = \sum_{\mathbf{i=1}}^{\mathbf{n}} \left(\mathbf{HQ_i} \times \sum_{\mathbf{j \neq i}}^{\mathbf{n}} \mathbf{f_{ij}}\, \mathbf{M_{ij}^{B_{ij}\theta_{ij}}} \right) \qquad 6$$

$$\mathbf{f_{ij}} = \frac{\mathbf{HQ_j}}{\mathbf{HI_{add}} - \mathbf{HQ_i}} \qquad 7$$

$$\theta_{ij} = \frac{\left(HQ_i \times HQ_j\right)^{0.5}}{(HQ_i + HQ_j) \times 0.5} \qquad 8$$

- HI_{int} = HI modified by binary interactions data; HQ_i = hazard quotient for chemical i ; f_{ij} = toxic hazard of the jth chemical relative to the total hazard from all chemicals potentially interacting with chemical i (thus j cannot equal i),; M_{ij} = interaction magnitude, the influence of chemical j on the toxicity of chemical I; B_{ij} = score for the strength of evidence that chemical j will influence the toxicity of chemical I; Θij = degree to which chemicals i and j are present in equitoxic amounts.

Results And Discussion

Calculated Risk estimate values of hypothetic exposure of BPA and DEHP(no mixture toxicity)

WATER TYPE	CONCENTRATION (µG/L)	ADD(µG/KG WT/D) (EQ 1A & 1B)		
			HQ(NON-CANCEROUS)	LCR(CANCEROUS)
NON-CANCEROUS EFFECTS BPA (RFD=50 µG/KGWT/D)				
DRINKING WATER	0.031	1.03×10^{-3}	2.06×10^{-5}	-
SURFACE WATER	21	0.035	7×10^{-4}	-
EFFECTS DUE TO DEHP (RFD=20 µG/KGWT/D; PF=1.4×10^{-2} /MG/KG/DAY)				
			HQ(NON-CANCEROUS)	LCR(CANCEROUS)
DRINKING WATER	8.780	0.293	0.0146	4.102×10^{-6}
SURFACE WATER	320	0.533	0.0267	7.462×10^{-6}

Calculated risk estimate values of exposure to plastic constituents mixture (Without interaction)

REFERENCE	EXPOSURE SCENARIO	CONCENTRATION		DEHP (RFD=20µG/KG WT/D)		BPA (RFD=50µG/KGWT/D)		HAZARD INDEX(NON-CANCEROUS)
		DEHP (µg/L)	BPA (µg/L)	ADD_1	HQ_1	ADD_2	HQ_2	
CASAJUAN AND LACORTE (2003)	INGESTION OF DRINKING WATER	0.134	0.01	0.004467	0.000223	0.005667	0.000113	0.000337
AMIRIDOU AND VOUTSA, (2011)	INGESTION OF DRINKING WATER	0.580	0.170	0.019333	0.000967	0.000333	6.67×10^{-6}	0.000973
FROMME ET AL.(2001)	INGESTION DURING SWIMMING	97.8	0.41	0.163	0.00815	0.683333	0.013667	0.021817
TRAN ET AL.(2015)	INGESTION DURING SWIMMING	1.7	0.79	0.002833	0.000142	1.316667	0.026333	0.026475

HQ for mixture of plastic constituents (Without Interaction) is <1,Hence water is safe with no risk.

Calculated risk estimate values of exposure of plastic constituents mixture (With interaction) Bij=Category I; $M_{12}=M_{21}=5$; $F_{12}=F_{21}=1$

Data Source	Exposure Scenario	HQ_1	HQ_2	$\theta_{ij}=\theta_{12}=\theta_{21}$	$B_{ij}=B_{12}=B_{21}$ (Category I)		$HI_{int}=\sum_{i=1}^{n}(HQ_i \times \sum_{j\neq i}^{n} f_{ij} M_{ij}^{B_{ij}\theta_{ij}})$	
					S	A	SYNERGISM	ANTAGONISM
CASAJUAN AND LACORTE (2003)	INGESTION OF DRINKING WATER	0.000223	0.000113	0.94511	1	-1	0.0015	7.34×10^{-5}
AMIRIDOU AND VOUTSA, (2011)	INGESTION OF DRINKING WATER	0.000967	6.67×10^{-6}	0.16495	1	-1	0.0013	0.000746
FROMME ET AL.(2001)	INGESTION DURING SWIMMING	0.00815	0.013667	0.96750	1	-1	0.1035	0.0046
TRAN ET AL.(2015)	INGESTION DURING SWIMMING	0.000142	0.026333	0.14590	1	-1	0.0335	0.0209

S- Synergism, A- Antagonism

HQ value is less than 1, hence no risk.

Calculated risk estimate values of exposure of plastic constituents mixture (With interaction) Bij Category II; $M_{12}=M_{21}=5$; $F_{12}=F_{21}=1$

DATA SOURCE	EXPOSURE SCENARIO	HQ_1	HQ_2	$\theta_{ij}=\theta_{12}=\theta_{21}$	$B_{ij}=B_{12}=B_{21}$ (Category II)		$Hi_{int}=\sum_{i=1}^{n}(HQ_i \times \sum_{j\neq i}^{n} f_{ij} M_{ij}^{B_{ij}\theta_{ij}})$	
					S	A	Synergism	Antagonism
CASAJUAN AND LACORTE (2003)	INGESTION OF DRINKING WATER	0.000223	0.000113	0.94511	0.75	-0.5	0.001054	0.000157
AMIRIDOU AND VOUTSA, 2011	INGESTION OF DRINKING WATER	0.000967	6.67×10^{-6}	0.16495	0.75	-0.5	0.001188	0.000852
FROMME ET AL.(2001)	INGESTION DURING SWIMMING	0.00815	0.013667	0.96750	0.75	-0.5	0.070142	0.010015
TRAN ET AL.(2015)	INGESTION DURING SWIMMING	0.000142	0.026333	0.14590	0.75	-0.5	0.031574	0.023542

S- Synergism, A- Antagonism

HI(Hazard Index) for plastic constituents is less than 1, which indicates no risk.

Knowledge Gap

HAZARD IDENTIFICATION

Suggested Actions

Knowledge Gap	Suggested Actions
Lack of Information about co-occurrence of chemicals	• Inventory of occurrence of chemicals in environment needs to be developed.
Combined toxicity information not available	• Toxicology research needs to be carried out for mixture of chemicals dosing.
No methodology to identify mixtures	• Monitoring of constituents simultaneously to determine chance of co-occurrence.

EXPOSURE ASSESSMENT

Knowledge Gap

Suggested Actions

Knowledge Gap	Suggested Actions
Aggregate effect of mixture through various routes of exposure	• More research needs to be done to understand combined effect from oral, dermal and inhalation route
Concentration of BPA and DEHP simultaneously in drinking water and surface water is limited.	• More laboratory and field monitoring data by collecting more samples and analyzing them.
Uncertainty exists in accuracy of exposure data.	• Application of new technology to epidemiology[44]. • Use of Biomarkers

Knowledge Gap

DOSE-RESPONSE ASSESSMENT

Suggested Actions

RfD value of mixture of chemicals is not available	• Monitoring and modeling needs to be done to derive combined RfD formula; • Create database to generate combined RfD value
Interaction type (synergism or antagonism)	• Information obtained from dose-response studies; information on toxicity mechanism; mode of action

RISK CHARACTERIZATION

Knowledge Gap	Suggested Actions
Interaction effect from cancerous and non-cancerous plastic constituents	• Research on combine effect of cancerous and non-cancerous plastic constituents.
Weight of evidence factor(B): Based on data made by group of experts; rough values; synergism and antagonism effect	• Some mathematical basis needs to be developed for estimating this factor; more information on combined effect.
Interaction magnitude(M): synergism and antagonism interaction not considered; generally taken as 5 but this does not have strong empirical background.	• More research on synergism and antagonism effect.

TOP THREE MAJOR GAPS

Risk can be calculated with maximum accuracy by using interaction formula if these gaps are filled

Information on Co-occurrence of plastic constituents

Uncertainty in determining Factor Bij (US EPA) used in Hazard index interaction Eq 6.

Uncertainty in determining Mij used in Hazard index interaction Eq 6.

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THANK YOU