Population Based Exposure Assessment of Bioaccessible Arsenic in Carrots

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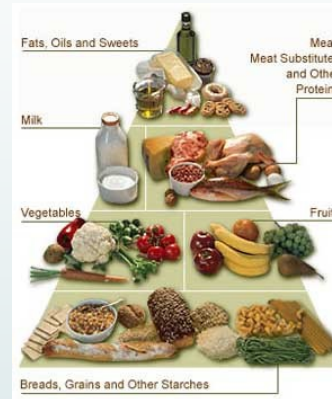
Introduction

Arsenic is classified as Type 1 carcinogen by IARC

Water

Food

Exposure routes are:
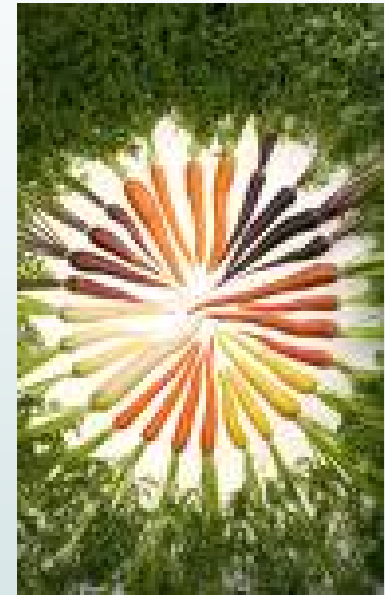

- Easy to analyze
- Centralized distribution
- Easy to control
- Mostly Inorganic arsenic
- Mostly bioaccessible

- Different matrices
- Origin unknown
- Not easy to control
- Different arsenic species in different foods
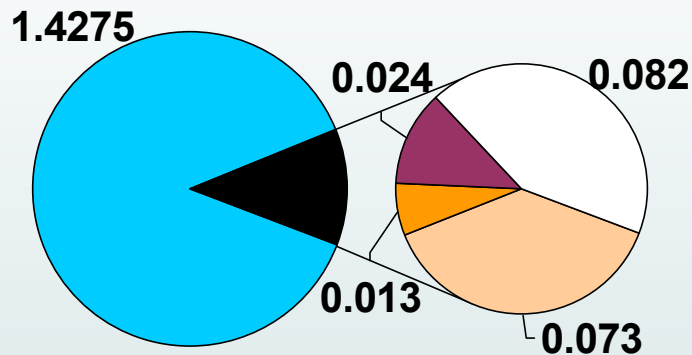- Bioaccessibility varies

Foods with High Arsenic Concentration

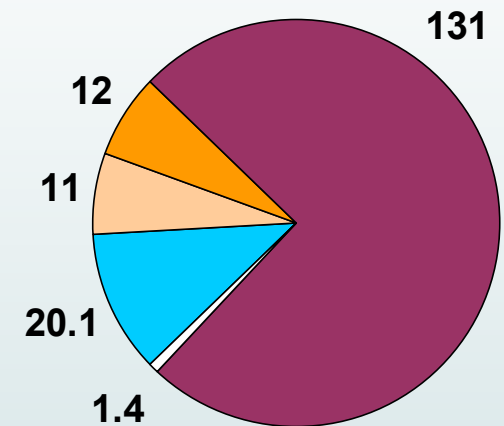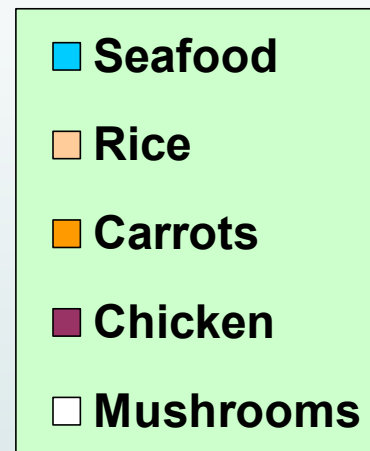
Source - Total Diet Study by FDA in 2004

Exposure

Average Total Arsenic Concentration (mg/kg)

Average Daily Consumption by U.S. Population (grams)

1.4275

0.024   0.082

0.013

0.073

🟦	**Seafood**
⬜	**Rice**
🟧	**Carrots**
🟥	**Chicken**
⬜	**Mushrooms**

131

12

11

20.1

1.4

Exposure = Concentration x Consumption

Exposure ≠ Dose

Outline

Exposure = Concentration X Consumption

Speciation of bioaccessible arsenic in carrots

Population based carrot consumption

Stochastic Human Exposure and Dose Simulation

Population based Exposure Assessment

Typical Sample Preparation for Exposure Analysis

Total Digestion

+
HNO_3
H_2O_2
+
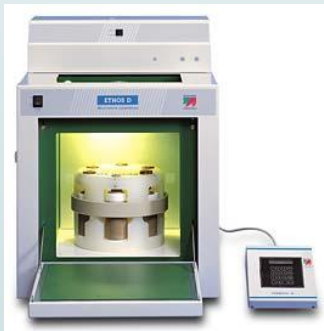
No Species Specific Information

Speciation Analysis

Chemical Based Extractions:
 Acid
 Base
 Water

Biological Relevance???

Sample Preparation that Approximates Pre-systemic Exposure

IDEAL
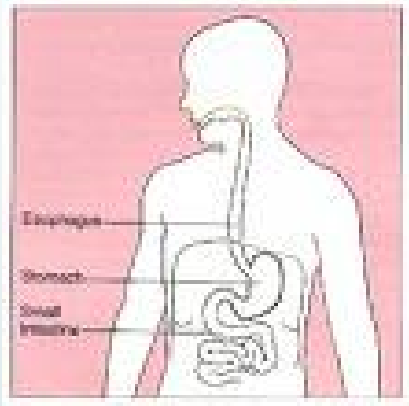
Alternatives

Tedious
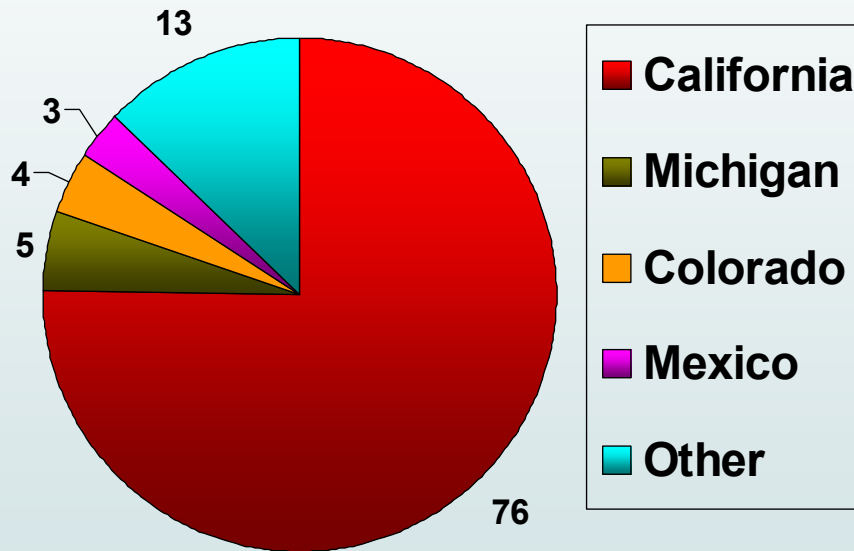
Cross-species correlation?

Ethical issues

In-vitro studies that mimic human GI system

Better control

Estimate of bioaccessible component

Sample Collection

Carrot Production Demographics

Carrot sampling for this study

Ground water Arsenic profile in USA
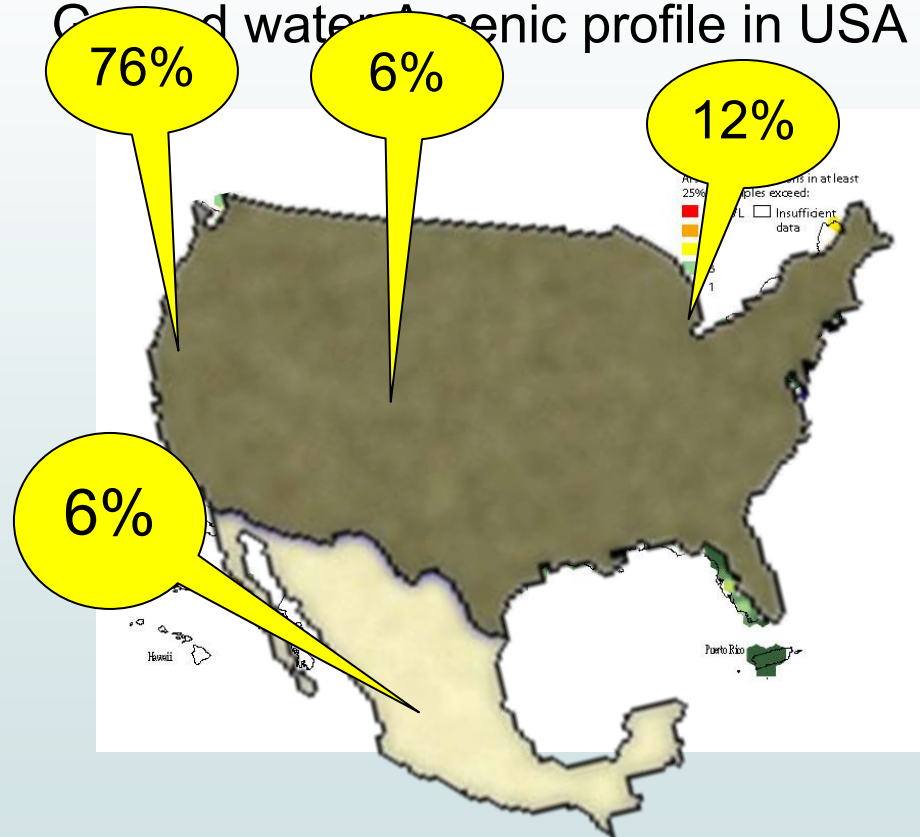
Sample Collection and Enzymatic Extraction

Carrot Samples Collected Based on Harvest Demographics

↓

Freeze Dried Carrot Samples

$As_{Total\ Digest}$ (As_{TD})

1. Rehydrate with DDI
2. Add saline solution, 5M HCl and pepsin
3. Place in 37°C waterbath with platform agitator for 1 hour

Carrot Sample after Synthetic Stomach Extraction

1. pH adjust to 6 with 1M $NaHCO_3$
2. Add pancreatin solution & 1M NaOH
3. Place in 37°C waterbath with platform agitator for 2 hours

Carrot Sample after Synthetic Intestine Extraction

↓

Enzymatic Carrot Sample

Sample Analysis

Enzymatic Carrot Sample

As$_{\text{Total Extract}}$ (As$_{\text{TE}}$)

Speciation Analysis ($\sum$As$_{\text{chrom}}$)

ArCl interference for As analysis

Collision cell facilitates this analysis

High temperature 27MHz plasma generator

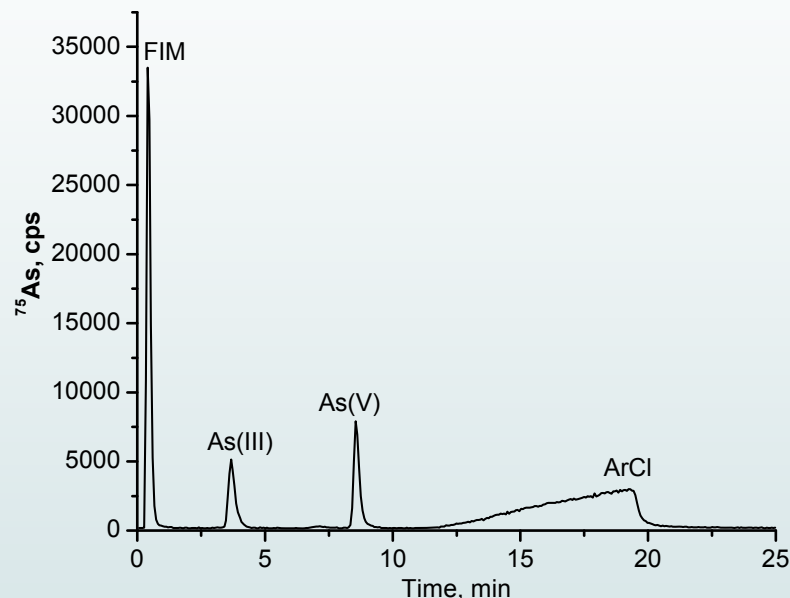Multi-element interference removal by on-axis octopole reaction cell

Fast simultaneous dual mode detector (9 orders dyn. range)

Low flow sample introduction system

High frequency hyperbolic quadrupole
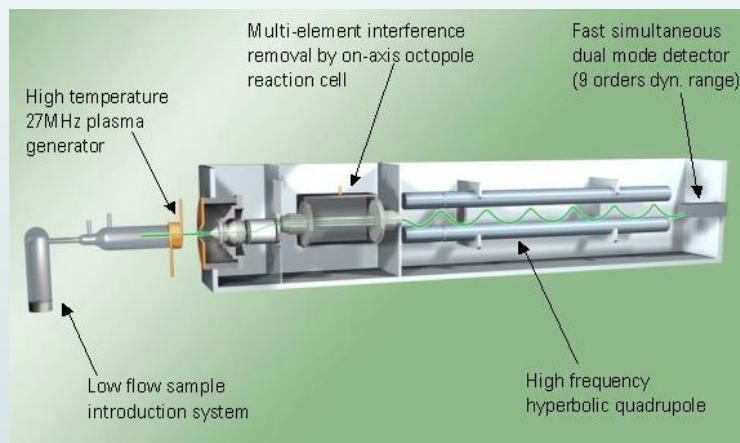
Pump	Agilent 1100 series
Column	PRP- X100 (PEEK, 4.6×250 mm) with guard column
Eluent	10 mM ammonium nitrate +10 mM ammonium phosphate
pH	4.5
Flow rate	1mL/min

Mass balance table for species specific bioacce-ssibility based analyses of arsenic in carrots

1	2	3	4	5	6	7	8	9
	As_{Total}				$As_{Speciation}$			
Sample	Wet Weight Moisture Content (%)	Dry Weight Total Digest (ng/g ± 2σ)	Wet Weight Total Digest (ng/g ± 2σ)	Dry Weight Extraction Efficiency (% ± 2σ)	Dry Weight $As_{Inorganic}$ (ng/g ± 2σ)	Wet Weight $As_{Inorganic}$ (ng/g ± 2σ)	Dry Weight Chromatographic Recovery (% ± 2σ)	Dry Weight Overall Recovery (% ± 2σ)
1	91	36 ± 0.8	3.5 ± 0.15	61 ± 11.0	21.4 ± 2.5	2.1 ± 0.2	87 ± 3.7	59 ± 6.9
2	90	37 ± 4.6	4.1 ± 1.03	62 ± 17.5	22.7 ± 2.0	2.5 ± 0.2	101 ± 59.1	61 ± 21.5
3	87	36 ± 4.7	5.4 ± 0.70	82 ± 27.2	28.0 ± 5.6	4.2 ± 0.8	92 ± 22.0	76 ± 15.1
4	90	58 ± 11.2	6.5 ± 1.25	87 ± 21.5	45.8 ± 14.2	5.1 ± 1.6	91 ± 19.6	79 ± 24.5
5	88	48 ± 4.2	6.6 ± 0.57	57 ± 22.0	28.3 ± 9.2	3.9 ± 1.3	103 ± 10.5	59 ± 19.1
6	87	43 ± 3.5	6.5 ± 0.52	69 ± 17.2	27.4 ± 3.8	4.1 ± 0.6	93 ± 16.7	64 ± 8.9
7	88	63 ± 1.7	8.6 ± 0.23	74 ± 18.2	49.1 ± 12.5	6.7 ± 1.7	107 ± 40.4	78 ± 19.9
8	89	74 ± 11.0	9.2 ± 1.35	77 ± 11.0	52.3 ± 8.3	6.5 ± 1.0	93 ± 28.0	71 ± 11.2
9	91	107 ± 1.3	10.5 ± 0.12	53 ± 9.0	72.0 ± 1.1	7.1 ± 0.1	127 ± 22.8	67 ± 1.0
10	90	63 ± 6.0	7.0 ± 0.65	72 ± 2.5	48.7 ± 4.0	5.4 ± 0.4	108 ± 5.6	77 ± 6.37
11	90	8 ± 5.4	0.85 ± 0.60	ND	ND	ND	ND	ND
12	90	79 ± 5.7	8.7 ± 0.63	69 ± 6.4	55.6 ± 4.5	6.2 ± 0.5	102 ± 2.2	70 ± 5.7
13	90	79 ± 5.4	9.0 ± 0.65	71 ± 24.2	62.5 ± 16.7	6.9 ± 1.9	112 ± 40.4	79 ± 21.1
14	90	24 ± 0.6	2.7 ± 0.07	48 ± 15	ND	ND	ND	ND
15	87	57 ± 5.9	8.5 ± 0.88	43 ± 9.0	27.9 ± 6.0	4.2 ± 0.9	114 ± 25.8	49 ± 10.6
16	90	116 ± 14.6	12.8 ± 1.61	29 ± 2.4	32.5 ± 1.5	3.6 ± 0.2	96 ± 8.0	28 ± 1.3
17	89	39 ± 1.3	4.8 ± 0.16	93 ± 56.6	32.4 ± 4.2	4.0 ± 0.5	94 ± 46.1	83 ± 10.9
18	90	43 ± 3.6	4.7 ± 0.39	43 ± 16.2	18.0 ± 7.1	2.0 ± 0.8	72 ± 14.0	42 ± 16.5
Across Matrix Avg ± 2σ	89 ± 2.6	56 ± 55	6.6 ± 5.9	56 ± 15	40 ± 31	4.8 ± 3.1	101 ± 21	65 ± 31

Across Matrix Averages

1	2	3	4	5	6	7	8	9
	As_{Total}				$As_{Speciation}$			
Sample	Wet Weight Moisture Content %	Dry Weight Total Digest (ng/g ± 2σ)	Wet Weight Total Digest (ng/g ± 2σ)	Dry Weight Extraction Efficiency (% ± 2σ)	Dry Weight $As_{Inorganic}$ (ng/g ± 2σ)	Wet Weight $As_{Inorganic}$ (ng/g ± 2σ)	Dry Weight Chromatographic Recovery (% ± 2σ)	Dry Weight Overall Recovery (% ± 2σ)
1								
18								
Across Matrix Avg ± 2σ	89 ± 2.6	56 ± 55	6.6 ± 5.9	56 ± 15	40 ± 31	4.8 ± 3.1	101 ± 21	65 ± 31

Outline

Exposure = Concentration X Consumption

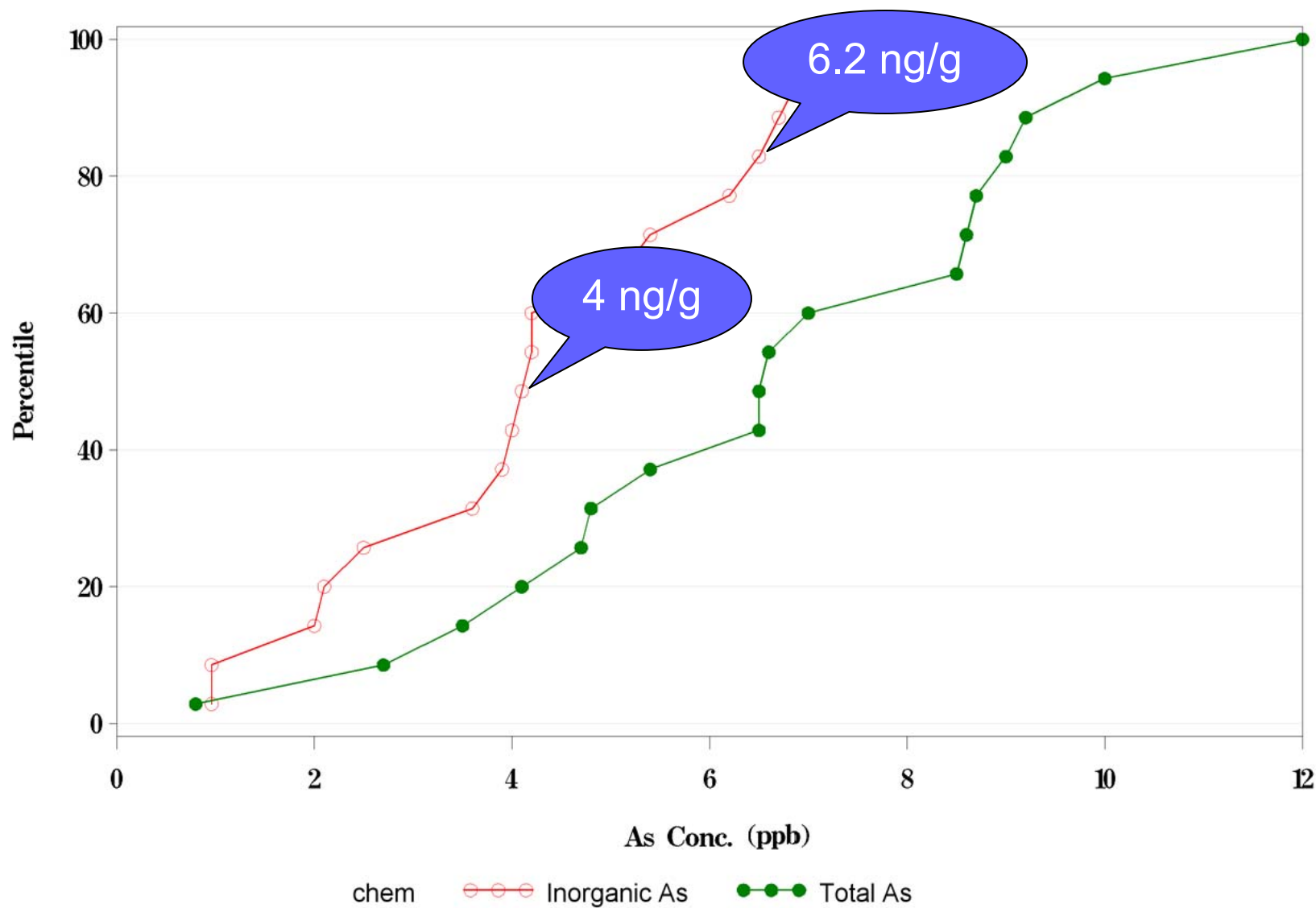Speciation of bioaccessible arsenic in carrots

Population based carrot consumption

Stochastic Human Exposure and Dose Simulation

Population Based Exposure Assessment

CDFs of Arsenic Concentration in Carrot

CDF-Cumulative distribution function

Population Based Carrot Consumption

- What We Eat In America (WWEIA), NHANES 2005-2006, considers 13,000 commonly eaten foods in US.

- 52,653 participants in the survey provided precise information of the food consumed by them.

- From the recipes of these foods consumed, the ingredient carrot is picked and calculated for consumption rate.

Outline

Exposure = Concentration X Consumption
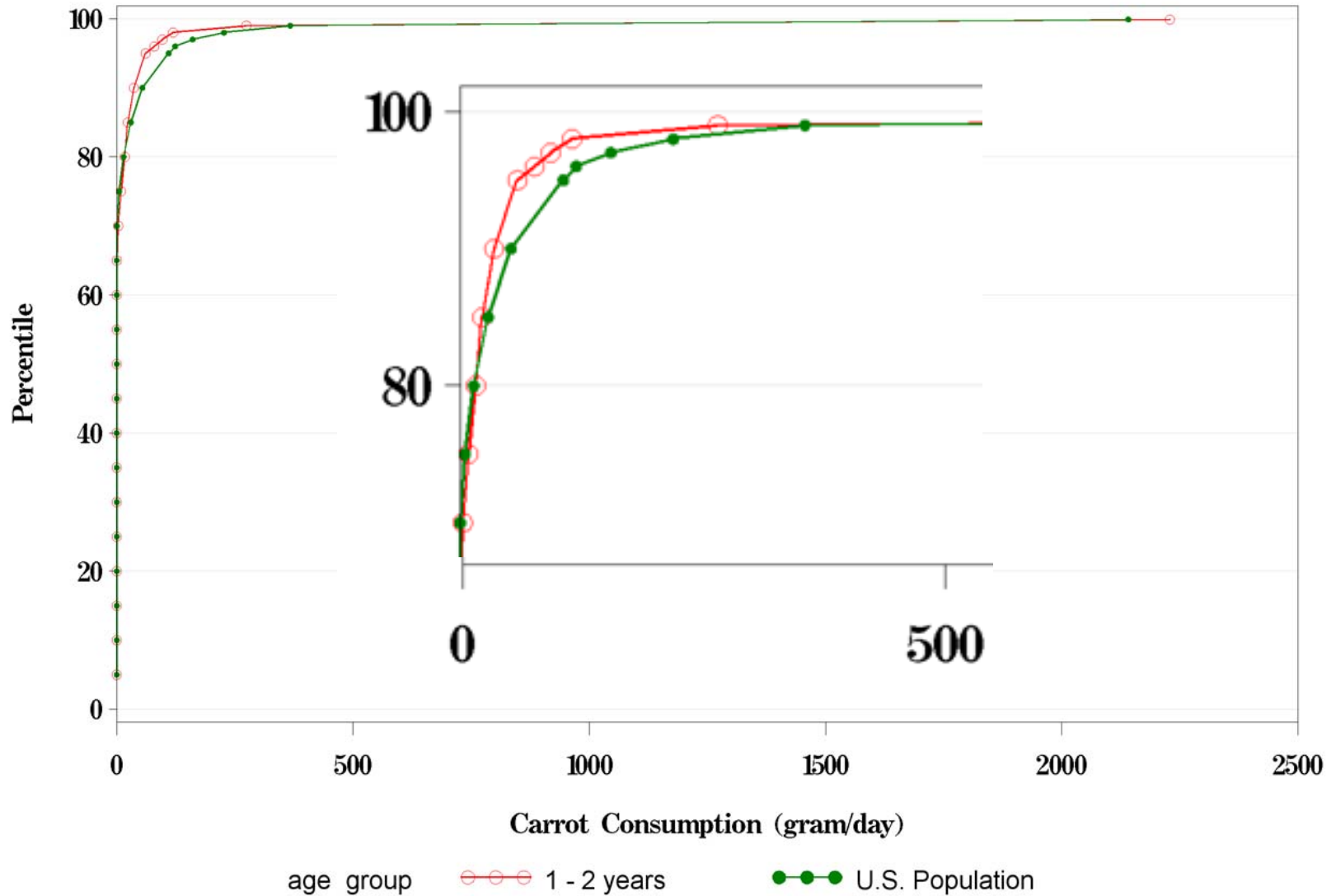
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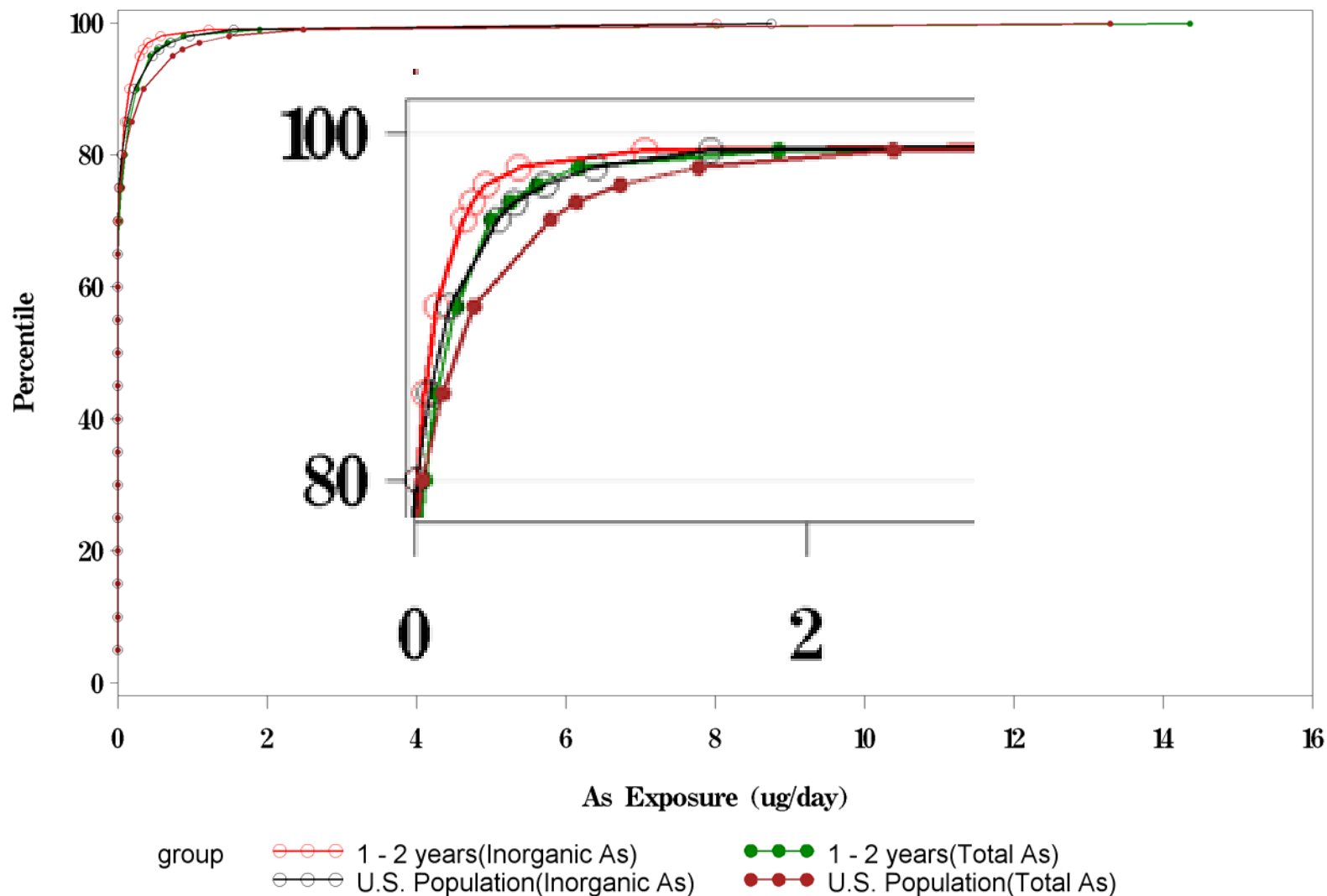
Population Based Exposure Assessment

CDFs of Carrot Consumption

Stochastic Human Exposure and Dose Simulation

- Probabilistic approach that involves both variability and uncertainty to predict distribution of a given exposure element.

- Population based exposure assessment for inorganic arsenic from carrots can be estimated.

CDFs of Arsenic Exposure

Explanation of Results

PTWI for inorganic arsenic is 0.015 mg/kg = 1.05 mg in a week or 1050 µg for 70 kg body weight

Population percentile	Carrot Consumed (g)	Total Arsenic (µg)	Inorganic Arsenic (µg)	% Contribution to PTWI
75th	35	0.2	0.13	0.01
95th	770	5.2	3.3	0.3

Explanation of Results

Population percentile	Carrot Consumed (g)	Total Arsenic (µg)	Inorganic Arsenic (µg)
75th	150	0.8	0.5
95th	475	3.0	2.0
99th	725	5.7	3.6

Weight of the baby in kg	% of Inorganic Arsenic exposure via carrots based on PTWI values		
	75th percentile consumption	95th percentile consumption	99th percentile consumption
7.7 (6.5 month old)	0.4	1.7	3.0
9.4 (10.5 month old)	0.3	1.4	2.5
10.6 (14.5 month old)	0.3	1.2	2.2
11.4 (18.5 month old)	0.3	1.2	2.0

Similarly….

Average Daily Consumption by U.S. Population (grams)

- Seafood
- Rice
- Carrots
- Chicken
- Mushrooms
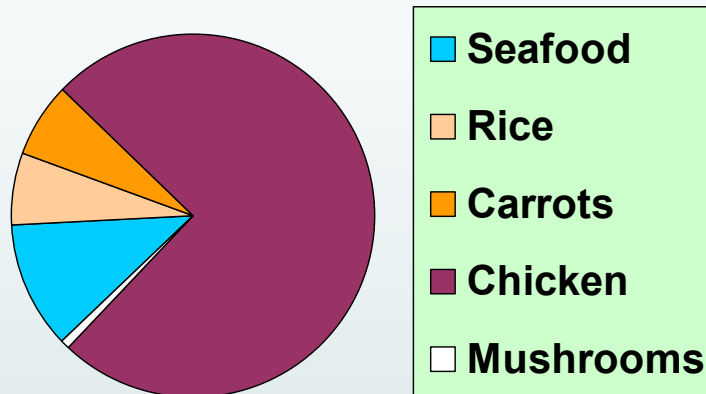
1. Sample collection representative of production demographics
2. Bioavailability based extractions
3. Food habits in a given population
4. Modeling studies that consider uncertainty and variability

Arsenic in Carrot Samples Analyzed

Total Arsenic
Inorganic Arsenic

Arsenic in Rice Samples Analyzed

Total Arsenic
Inorganic Arsenic

Rice data courtesy Heather Trenary
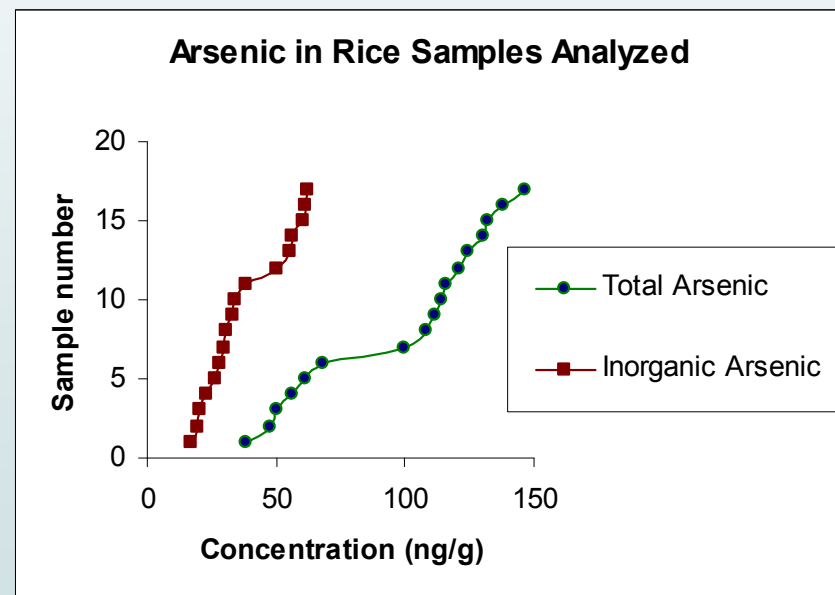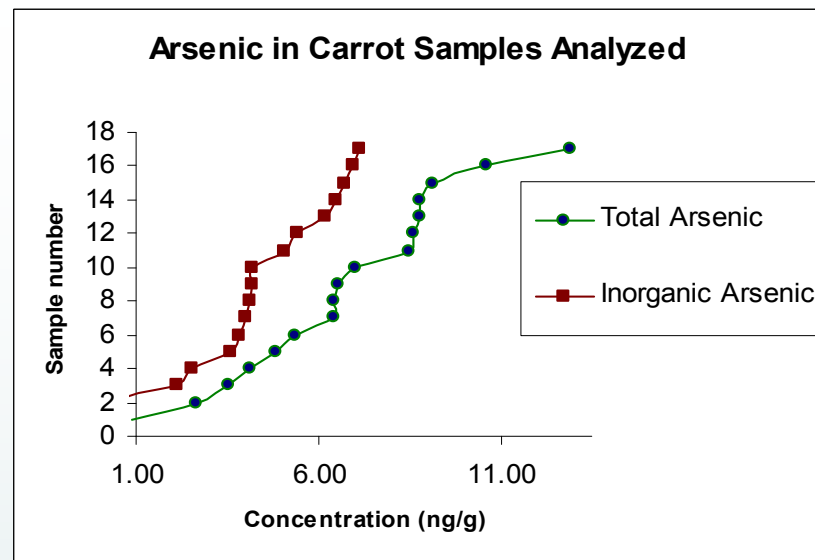
Conclusions

- Concentration of Arsenic in carrots was not dependent on geographic location

- Inorganic Arsenic is the only arsenic species found in carrots analyzed

- Concentration of As_{Total} ranges from 2 – 10 ng/g while that of As_{Inorg} ranges from 2 – 7 ng/g of carrot

- Carrots contribute to less than 0.3% of PTWI of inorganic arsenic in average adults

- Carrots contribute to less than 4% of PTWI of inorganic arsenic even in high exposure cases (infant)

Acknowledgments

- Dr. Jack Creed
- Dr. Jianping Xue
- Members of Dr. Jack Creed's group
- U.S. EPA
- Metallomics Organizers
- Dr. Joe Caruso
- Audience