

UNIVERSITY OF ILLINOIS CHICAGO

American Indian Medicinal Plants for Menopause: Collaboration with Urban Indigenous Women

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Age-Friendly in American Indian Elders
University of North Dakota School of Medicine and Health Sciences
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Land Acknowledgement

Disclosure

I do not have any relevant financial disclosures in relation to the content of this presentation.

1

Review the reasons for the decline of pharmaceutical treatments and rise of botanical treatments for menopausal symptoms

2

Use provided resources to help identify traditional American Indian medicinal plants

3

Discuss highest selling botanical herbs efficacy for menopause that were/are used by American Indian tribes

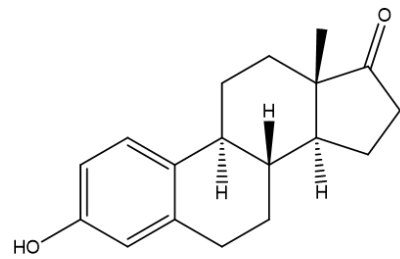
4

Describe a community based participatory research model that helped tell the story of traditional American Indian medicinal plants potential activity

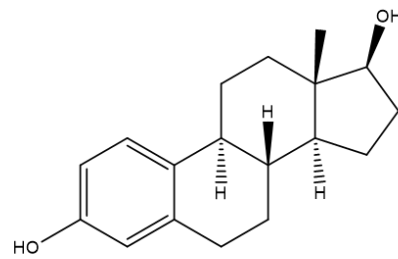
Learning Objectives

Women's Health and Hormonal Balance

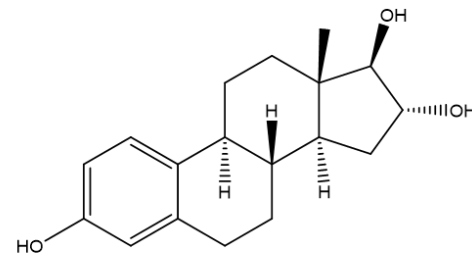
- Women may deal with unique gender specific health issues
- In some cases, these issues are regulated by hormones
- Hormones are chemical messengers
- Balancing of sex hormones, estrogen and progesterone are important for women's health
- Estrogen is one of the main sex hormone discussed for maintaining women's health



Estrone-E1



Estradiol-E2



Estriol-E3

Physiological Changes with Menopause

- Menopause → low levels of estrogen

- Symptoms

 - Vasomotor symptoms

 - Hot flashes

 - Night Sweats

 - Vaginal Atrophy

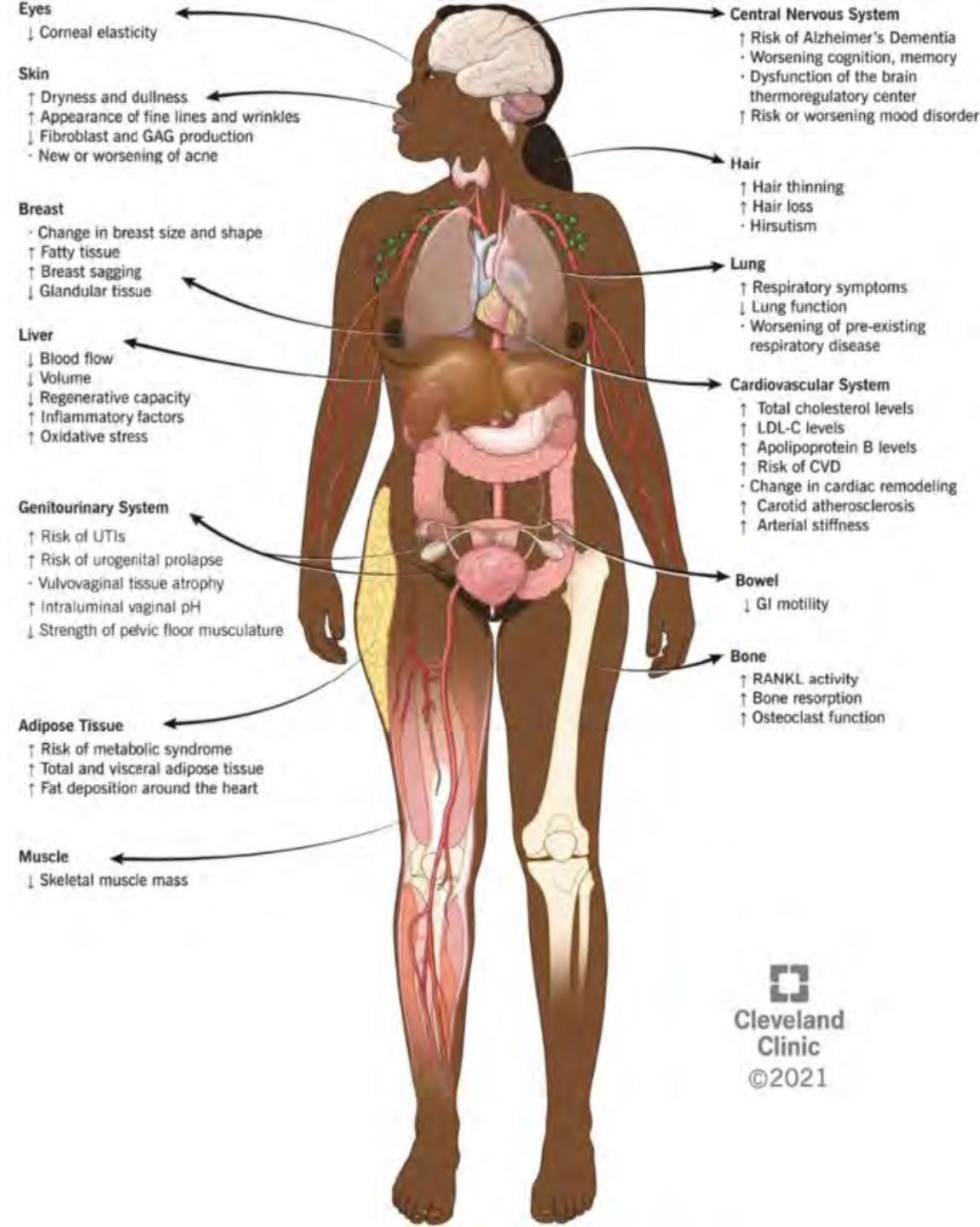
 - Mood Swings

- Hormone Therapy: Prempro (estrogen + progestin)

 - Reduced hot flashes

 - Insomnia

 - Hip fractures



Decline in Hormone Therapy

- Women's Health Initiative (WHI) Study: 1997-2002
 - >16,000 healthy, postmenopausal women aged 50-79 years
 - Examined Placebo vs. Prempro
 - Planned for 8 years, stopped after 5.2 years
 - Adverse outcomes
 - 26% increase in breast cancer
 - 29% increase in heart attacks
 - 41% increase in stroke
 - 22% increase in total cardiovascular disease

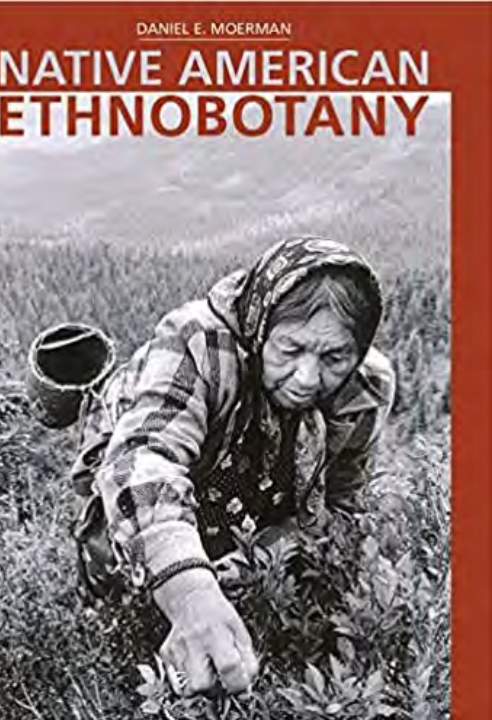


Ethnobotany

Ethnobotany is the study of humans' interactions with plants

- Food
- Religious practices
- Shelter
- Recreation
- Medicinal
 - **Medical ethnobotany is the study of traditional knowledge and practices of plants for medicinal purposes**





American Indian Ethnobotany

Native American Ethnobotany DB Home Search Uses Tribes Species About Contact

Native American Ethnobotany

A Database of Foods, Drugs, Dyes and Fibers of Native American Peoples, Derived from Plants.

Search the database

The database of ethnobotanical uses can now be searched using two different methods. A traditional text search provides basic text searching with experimental Boolean search features. A 'filtered' search allows you to select multiple attributes of the data to filter the search results.

Text search string:

[Filtered search form...](#)



<http://naeb.brit.org/>

UIC/NIH Botanical Center: Discovering Alternatives to Hormone Therapy and Chemopreventive Compounds

- Identify and test botanical alternatives for improving menopausal symptoms and hormonal chemoprevention activity
- Traditionally used by American Indians



Top Selling Herbal Supplements in 2020 are Traditionally Used by Indigenous Americans



Table 4. Top-Selling Herbal Supplements in 2020 — US Mainstream Multi-Outlet Channel

Rank	Primary Ingredient	Latin Binomial	Total Sales	% Change from 2019
1	Elder berry	<i>Sambucus nigra</i> and <i>S. canadensis</i>	\$275,544,691	150.3%
2	Horehound	<i>Marrubium vulgare</i>	\$137,054,571	-11.4%
3	Cranberry	<i>Vaccinium macrocarpon</i>	\$101,339,826	12.9%
4	Turmeric ^a	<i>Curcuma longa</i>	\$96,971,371	3.1%
5	Apple cider vinegar	<i>Malus</i> spp.	\$79,257,715	133.8%
6	Ginger	<i>Zingiber officinale</i>	\$64,779,632	39.3%
7	Echinacea ^b	<i>Echinacea</i> spp.	\$57,345,210	36.8%
8	Garlic	<i>Allium sativum</i>	\$42,924,030	12.1%
9	Fenugreek	<i>Trigonella foenum-graecum</i>	\$35,148,440	5.5%
10	Wheatgrass / Barley grass	<i>Triticum aestivum</i> / <i>Hordeum vulgare</i>	\$32,887,254	9.2%
11	Saw palmetto	<i>Serenoa repens</i>	\$32,697,628	5.4%
12	Ashwagandha	<i>Withania somnifera</i>	\$31,742,304	185.2%
13	Green tea	<i>Camellia sinensis</i>	\$31,408,078	-7.9%
14	Ivy leaf	<i>Hedera helix</i>	\$29,581,801	-32.0%
15	Ginkgo	<i>Ginkgo biloba</i>	\$28,576,480	9.7%
16	Cannabidiol (CBD)	<i>Cannabis sativa</i>	\$26,551,872	-30.0%
17	Black cohosh	<i>Actaea racemosa</i>	\$24,890,605	-12.0%
18	Beta-sitosterol ^c	—	\$24,827,065	52.3%
19	Red yeast rice ^d	<i>Oryza sativa</i>	\$24,613,191	-3.9%
20	Aloe	<i>Aloe vera</i>	\$24,403,736	11.2%
21	St John's wort	<i>Hypericum perforatum</i>	\$23,890,515	0.3%
22	Flax seed / Flax oil	<i>Linum usitatissimum</i>	\$22,150,127	-3.2%
23	Milk thistle	<i>Silybum marianum</i>	\$19,823,644	8.4%
24	Yohimbe	<i>Pausinystalia johimbe</i> syn. <i>Corynanthe johimbe</i>	\$17,774,381	-3.7%
25	Goji berry	<i>Lycium</i> spp.	\$16,104,457	15.9%
26	Valerian	<i>Valeriana officinalis</i>	\$14,596,855	-11.2%
27	Horny goat weed	<i>Epimedium</i> spp.	\$14,546,366	1.6%
28	Bioflavonoid complex ^e	—	\$14,137,366	-4.2%
29	Beet root	<i>Beta vulgaris</i>	\$13,945,332	22.4%
30	Cinnamon	<i>Cinnamomum</i> spp.	\$12,339,671	-18.2%
31	Senna ^f	<i>Senna alexandrina</i>	\$12,295,396	1.0%
32	Green coffee extract	<i>Coffea arabica</i>	\$12,263,598	-21.1%
33	Plant sterols ^g	—	\$11,498,813	4.3%
34	Ginseng	<i>Panax</i> spp.	\$11,200,292	-11.9%
35	Chamomile	<i>Matricaria chamomilla</i> syn. <i>M. recutita</i>	\$10,624,567	30.1%
36	Garcinia	<i>Garcinia gummi-gutta</i>	\$10,618,783	-35.7%
37	Fennel	<i>Foeniculum vulgare</i>	\$10,101,137	9.2%
38	Maca	<i>Lepidium meyenii</i>	\$10,075,136	21.8%
39	Açai	<i>Euterpe oleracea</i>	\$9,835,442	10.4%
40	Rhodiola	<i>Rhodiola</i> spp.	\$8,433,070	-4.3%

Black Cohosh

- Latin Name and Plant Part Used: *Actaea/Cimicifuga racemosa*; root and rhizome
- Other Common Names: Snakeroot, black bugbane, rattleweed, rheumatism weed
- Current Market Use: Menopause support



Black Cohosh

- Traditional Tribal Use and Preparation
 - Cherokee
 - Delaware
 - Iroquois
 - Micmac
 - Penobscot

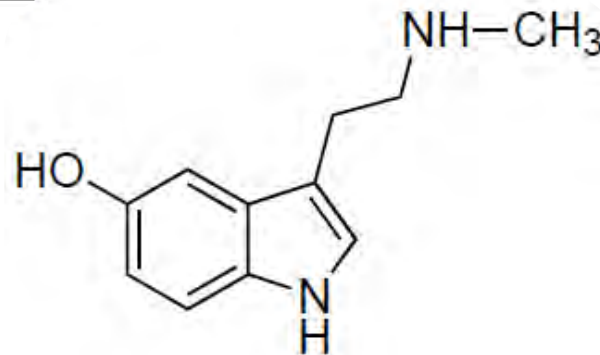
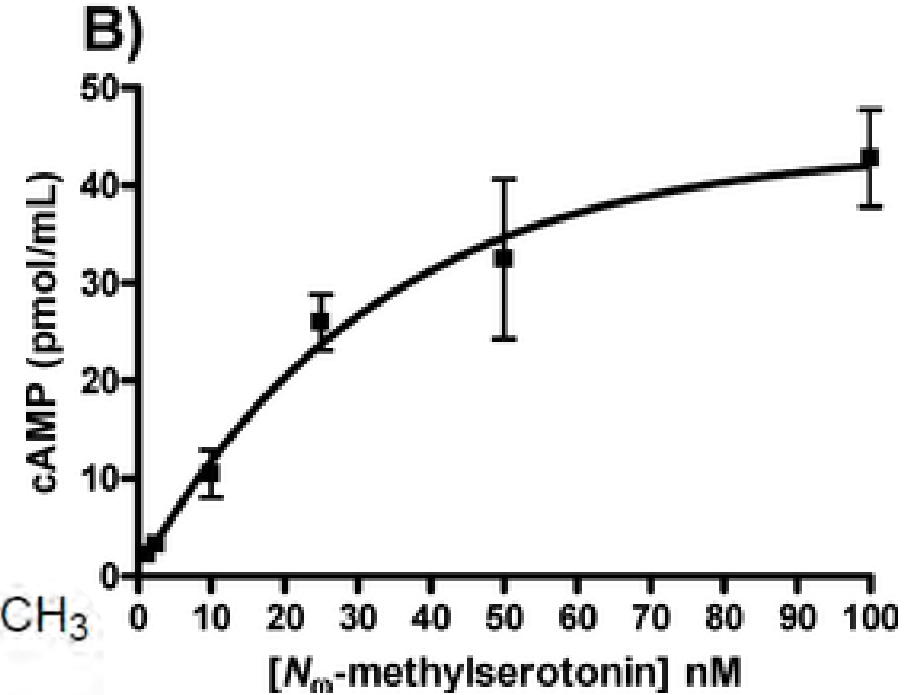
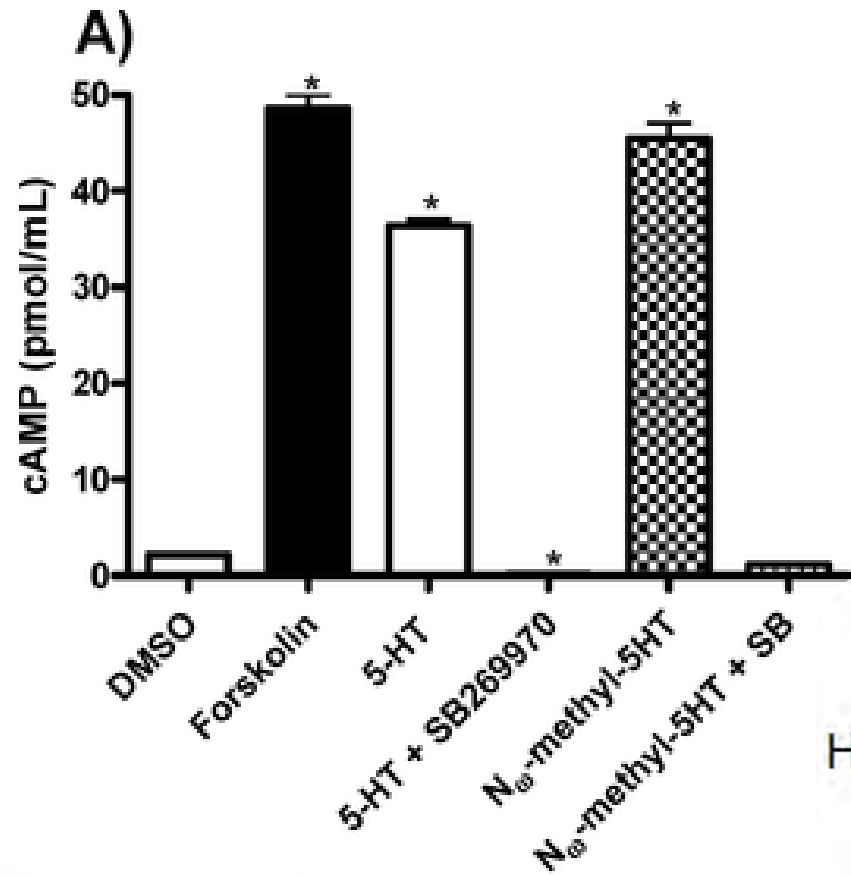


Black Cohosh

- Laboratory Research:
 - Active ingredients and potential mechanisms of action are still unknown
 - No estrogenic activity *in vitro* or *in vivo*
 - Selective estrogen receptor modulator (SERM)
 - Selective serotonin reuptake inhibitors (SSRIs)

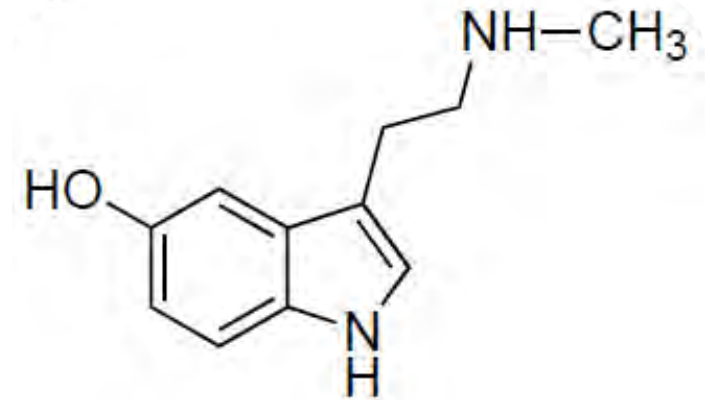
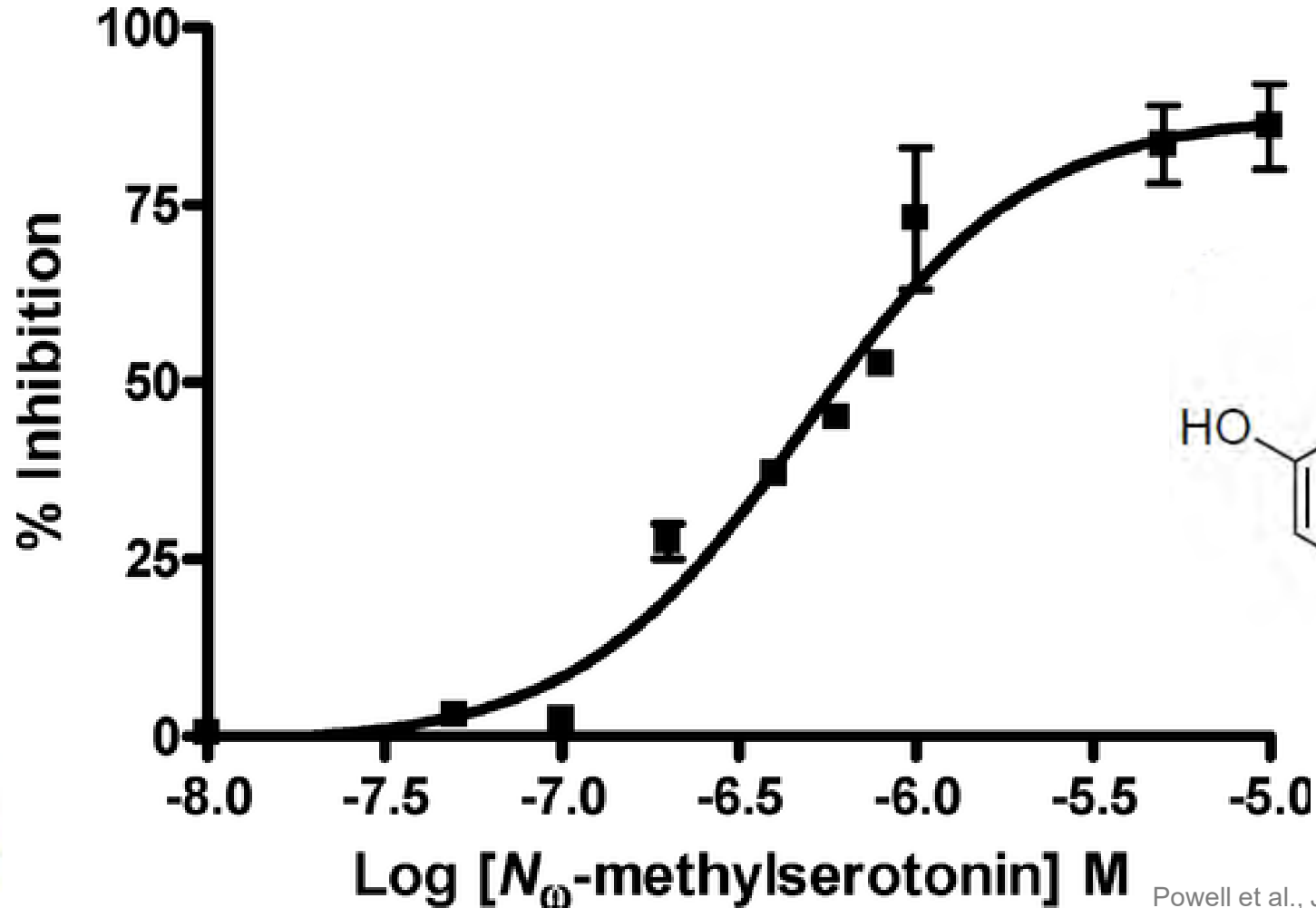


Black Cohosh Potential Serotonin Activity



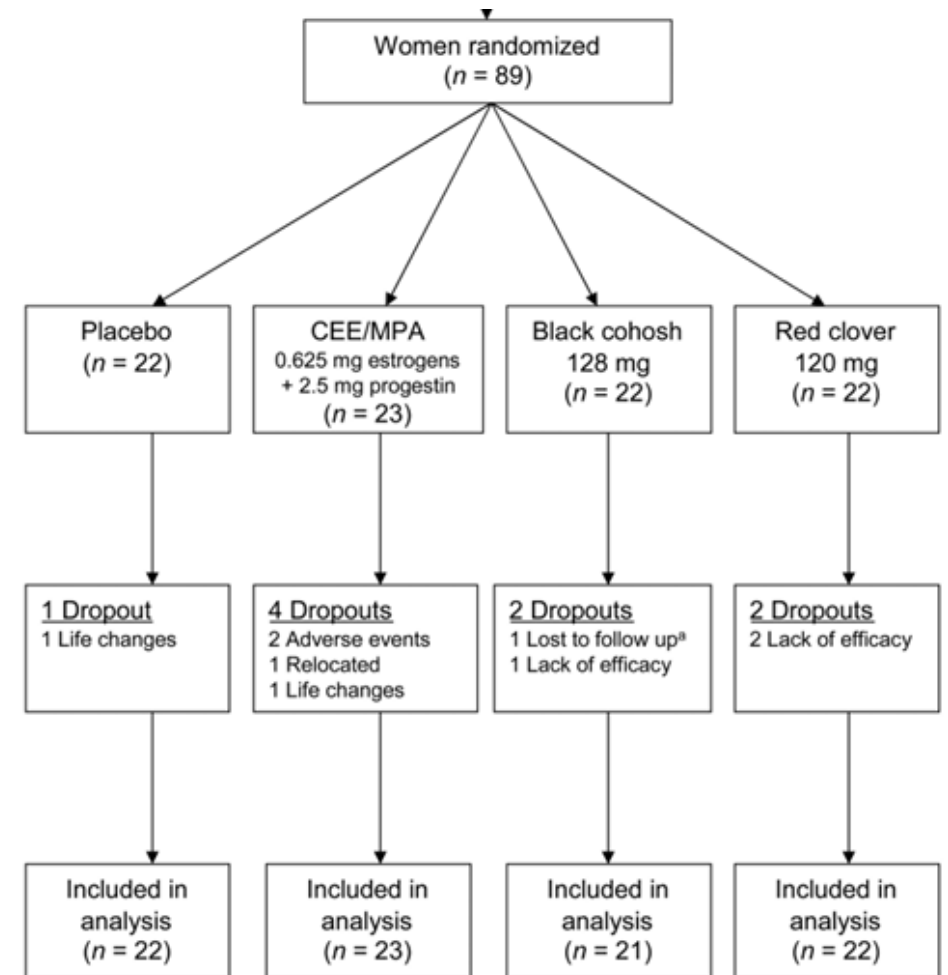
5-Hydroxy-N ω -methyltryptamine

Black Cohosh Potential Serotonin Activity



Clinical Investigation with Black Cohosh at UIC/NIH Botanical Center

- Goal: Safety and efficacy of daily administration of standardized extracts of black cohosh and red clover vs. placebo
- Study Design: Randomized, four arm, double blind; placebo-controlled, positive control → conjugated quine estrogens/medroxyprogesterone acetate
- Study Duration: 12 months
- Primary Outcome Measures: Reduction in vasomotor symptoms
- Secondary Outcomes Measures: Safety evaluation, reduction of somatic symptoms, relief of sexual dysfunction, overall improvement of quality of life



Baseline Demographics

	Placebo <i>n</i> =22	CEE/MPA <i>n</i> =23	Black Cohosh <i>n</i> =21	Red Clover <i>n</i> =22	All <i>n</i> =88	<i>P</i>
Mean age (SD), y	52.0 (4.2)	53.3 (4.0)	54.4 (3.9)	52.4 (4.6)	53 (4.2)	0.24
Mean BMI (SD), kg/m ²	30.1 (4.9)	26.0 (3.9)	28.3 (4.5)	30.5 (4.3)	28.7 (4.7)	0.004^a
Race, <i>n</i> (%)						0.005^{a,b}
African American	16 (72.7%)	7 (30.4%)	8 (38.1%)	13 (59.1%)	44 (50.0%)	
White	5 (22.7%)	16 (69.6%)	13 (61.9%)	5 (22.7%)	39 (44.3%)	
Hispanic	1 (4.6%)	-	-	3 (13.6%)	4 (4.5%)	
Pacific islander	-	-	-	1 (4.6%)	1 (1.1%)	
Past hormone use, <i>n</i> (%)	10 (45.5%)	10 (43.5%)	9 (40.9%)	10 (45.5%)	39 (43.8%)	0.99
Previous tobacco use, <i>n</i> (%)	8 (36.4%)	15 (65.2%)	13 (59.1%)	9 (40.9%)	46 (51.7%)	0.13
Alcohol use ^c	1.0 (1.6)	1.5 (1.9)	1.7 (1.9)	1.1 (1.3)	1.3 (1.7)	0.48
Last menstrual period, number of years (SD)	2.8 (2.9)	3.6 (2.9)	3.4 (2.6)	4.1 (2.8)	3.5 (2.8)	0.52
Gravida, <i>n</i> (SD)	2.7 (1.6)	2.1 (1.9)	2.4 (2.0)	3.0 (2.9)	2.6 (2.1)	0.53
No. deliveries (SD)	1.6 (1.0)	1.4 (1.3)	1.5 (1.3)	2.4 (2.4)	1.7 (1.6)	0.12
Endometrial thickness (SD)	4.6 (2.1)	3.8 (2.3)	3.7 (1.3)	3.9 (2.0)	3.8 (1.8)	0.66
Total cholesterol (SD)	200.1 (30.4)	217.8 (37.0)	221.8 (36.8)	209.2 (44.3)	213.2 (39.3)	0.10
Estradiol (SD)	29.7 (19.2)	24.3 (10.5)	26.8 (13.0)	27.9 (13.2)	27.1 (14.2)	0.45
FSH (SD)	79.1 (36.3)	99.3 (38.7)	86.0 (26.8)	70.1 (27.6)	84.8 (33.7)	0.08

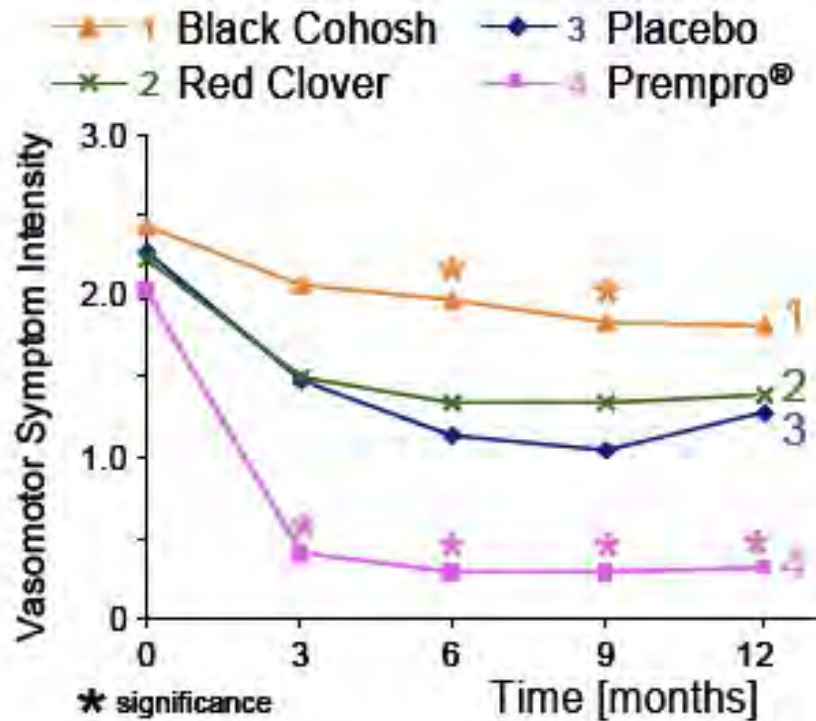
CEE, conjugated equine estrogens; MPA, medroxyprogesterone acetate; BMI, body mass index; FSH, follicle-stimulating hormone.

^aStatistically significant difference between groups.

^b*P* value for race from χ^2 test for overall homogeneity of race.

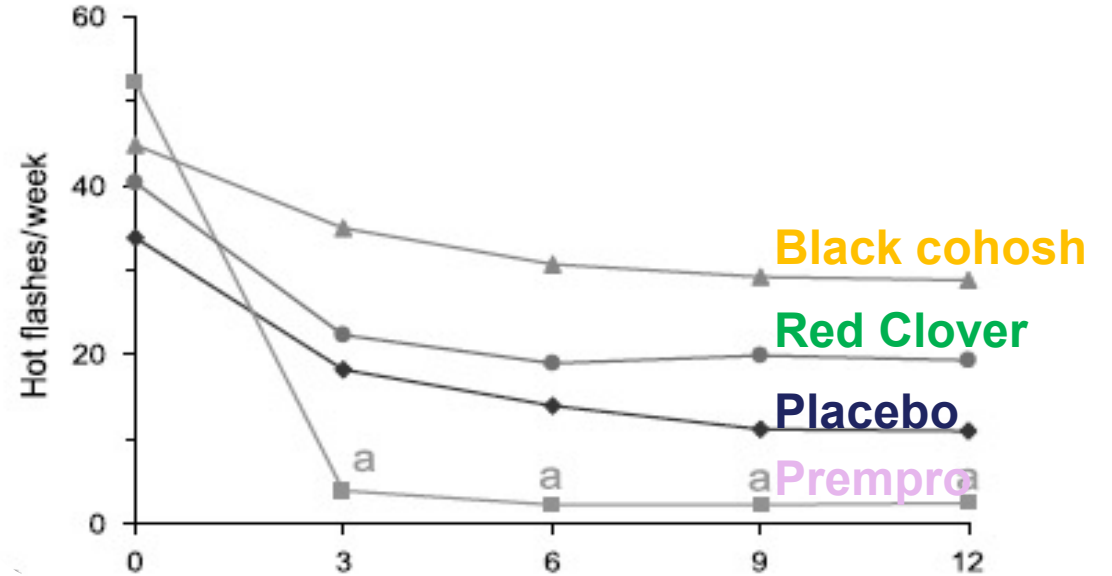
^cReported as number of drinks per week (SD).

Black Cohosh or Red Clover did not significantly improve menopausal symptoms



Reduction of hot flashes intensity:

- All treatments reduced intensity
- At 6 and 9 month: **Black cohosh** group showed higher symptom intensity compared with placebo ($p < 0.05$).



Reduction in hot flash frequency:

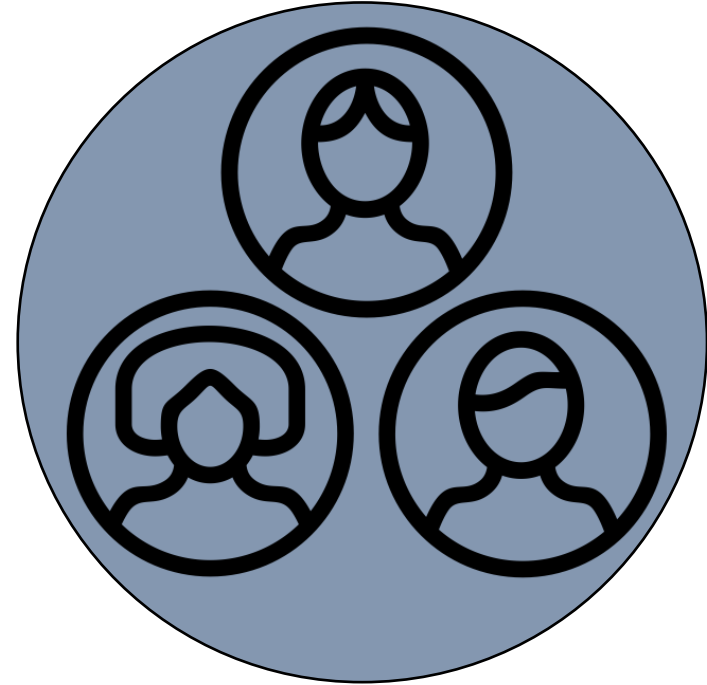
- **Black cohosh: 34%**
- **Red clover: 57 %**
- **Placebo: 63%**
- **Prempro: 94% ($p < 0.05$)**

Safety Evaluation of Black Cohosh

- Considered Safe
- No influence on:
 - Endometrial thickness or hormones
 - Liver parameters
 - Prothrombin time
- Worldwide at least 83 case reports concerning liver damage
- Safety review: Black cohosh products should be labeled to include a cautionary statement regarding liver safety.
- No known interactions with medications

Pharmacognosy and Medical Ethnobotany Research with Urban American Indian Women

From Benchwork to Community



Aim 1: Pharmacognosy

Identify estrogenic extracts and compounds from traditionally used American Indian plant species

Aim 2: Ethnobotany

- A. Identify current uses of the tested plants by urban American Indian women
- B. Understand how urban American Indian women perceive and experience menopause

The Benchmark

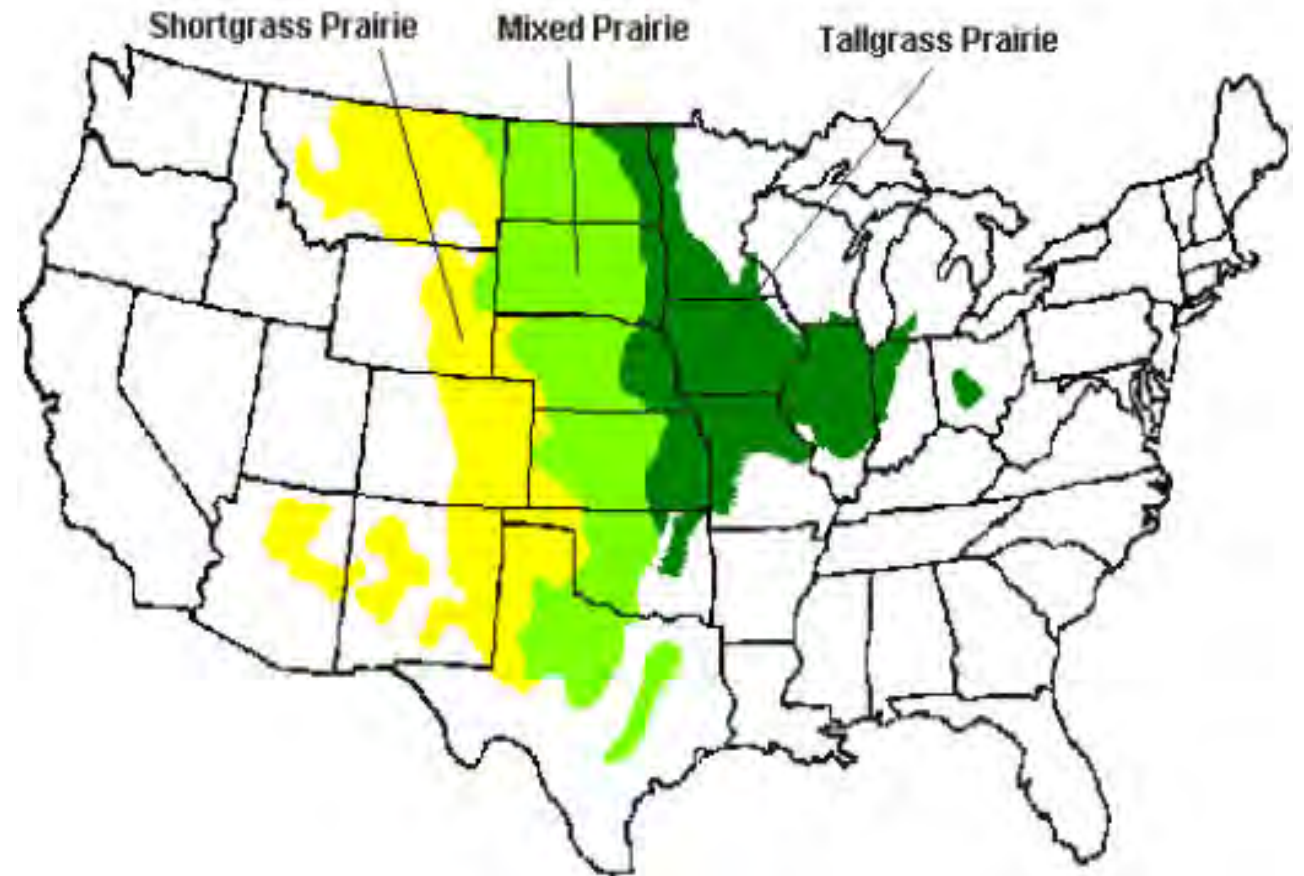


Aim 1: Pharmacognosy

Identify estrogenic extracts and compounds from traditionally used American Indian plant species

Tallgrass Prairie Plants from the Chicago Botanic Garden

- MOA established in 2005
- Study Illinois native plants for women's health
 - Some of these plants are considered at risk
- Over 400 samples
- 164 plant species



Screened 15 Chicago Botanic Garden Plant Samples to Identify Active Plants



Proserpinaca palustris L.
Marsh mermaidweed



Dasistoma macrophylla (Nutt.) Raf.
Mullein foxglove



Lithospermum canescens (Michx.) Lehm.
Hoary puccoon



Ruellia humilis Nutt.
Fringeleaf wild petunia



Amorpha canescens Pursh
Leadplant



Silphium perfoliatum L.
Cup plant



Chamaecrista fasciculata (Michx.) Greene
Partridge pea



Oenothera macrocarpa Nutt.
Bigfruit evening primrose



Echinoystis lobata (Michx.) Torr. & A. Gray
Wild cucumber



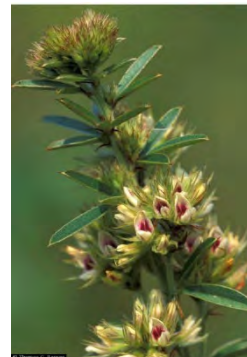
Symphyotrichum oblongifolium (Nutt.) G.L. Nesom
Aromatic aster



Desmanthus illinoensis (Michx.) MacMill
Bundleflower



Ludwigia alternifolia L.
Seedbox



Lespedeza capitata Michx.
Roundhead lespedeza



Stenaria nigricans Terrell
Florida diamond flowers



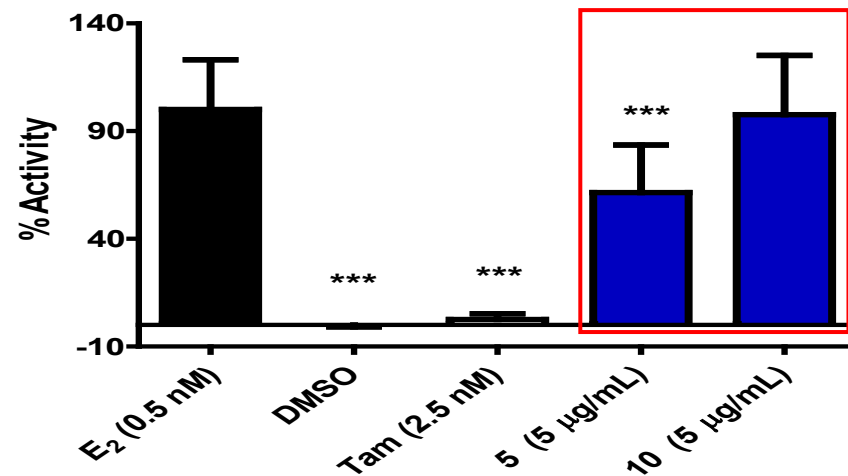
Verbena stricta Vent.
Hoary verbena

Three Active Plants in Ishikawa Estrogenicity Assay

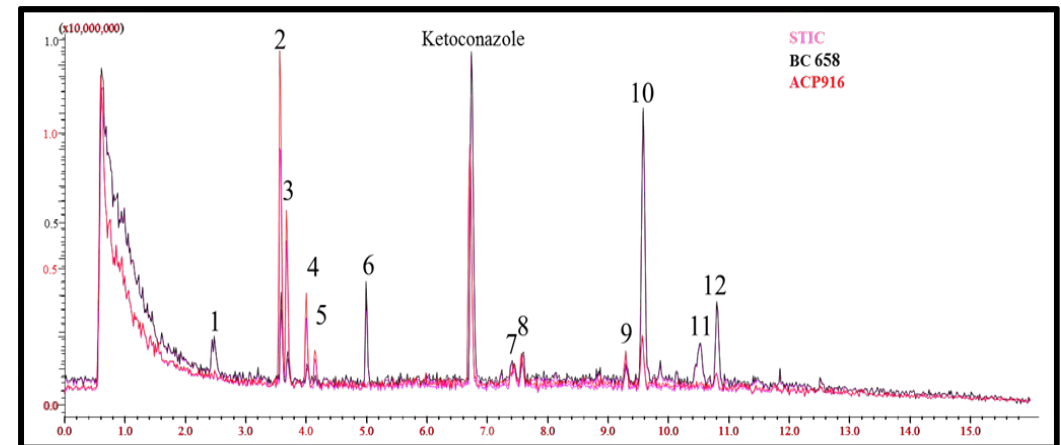
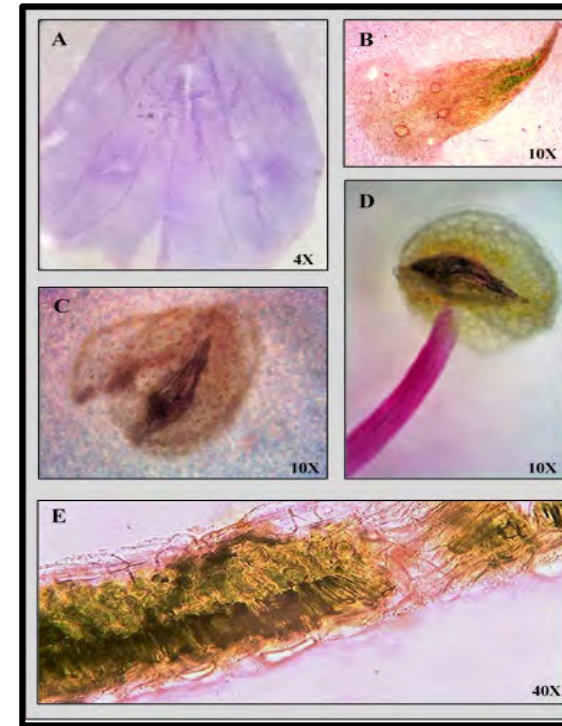


Sample	Estrogenic%	SD	Anti-Estrogenic%	SD	Cytotoxicity%	SD
Blank	1	± 0	1	± 0	13	± 4
DMSO	0	± 0	0	± 11	0	± 3
E ₂ (0.5nM)	100	± 7	-19	± 15	-7	± 6
4-OH Tamoxifen (5μM)	5	± 1	95	± 2	9	± 7
Leadplant (20 μg/mL)	1	± 0	85	± 7	49	± 3
Cup plant (20 μg/mL)	1	± 0	30	± 5	7	± 7

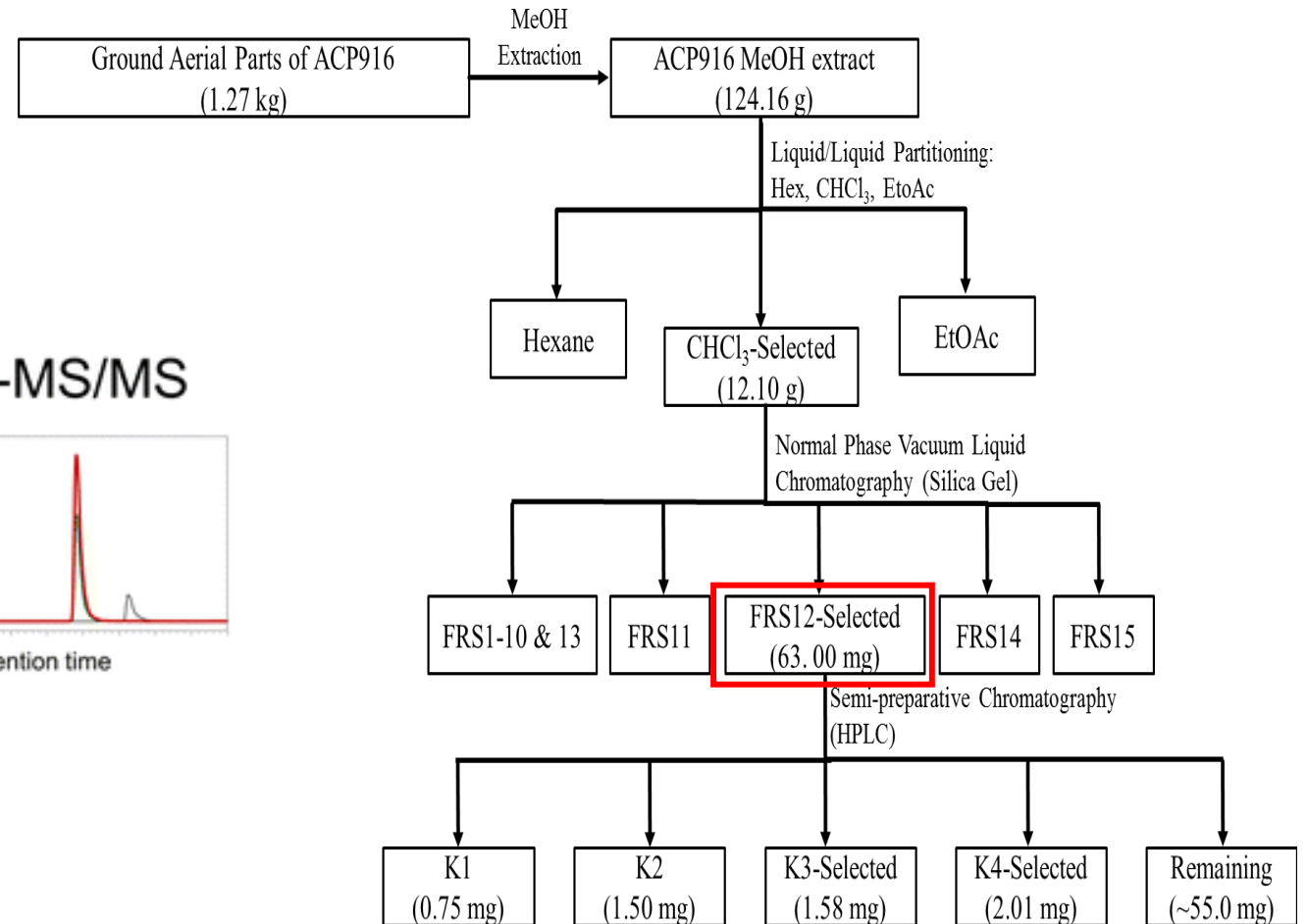
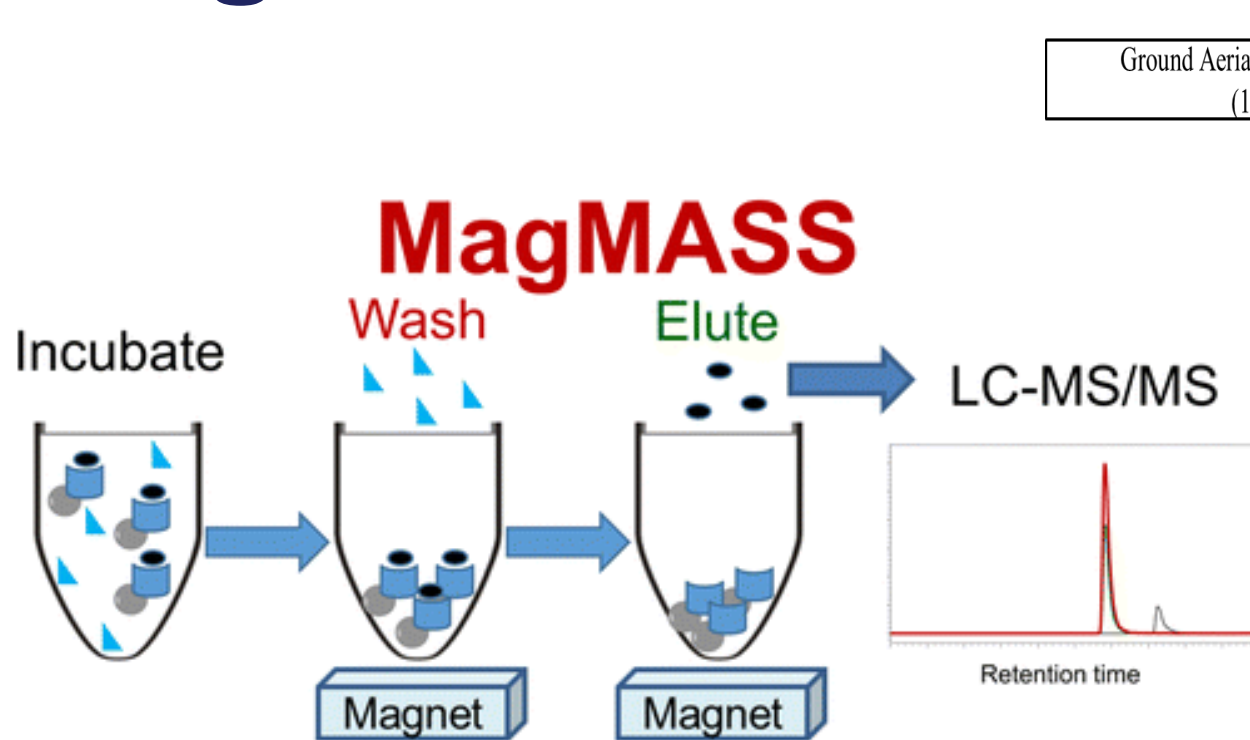
Estrogenic Activity of Roundhead Lespedeza

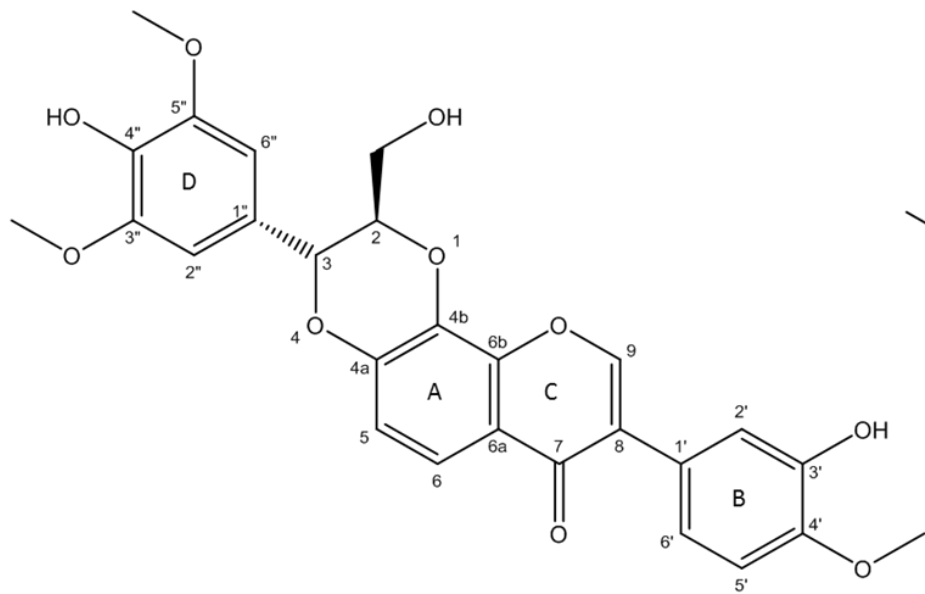


Recollected and Verified Leadplant

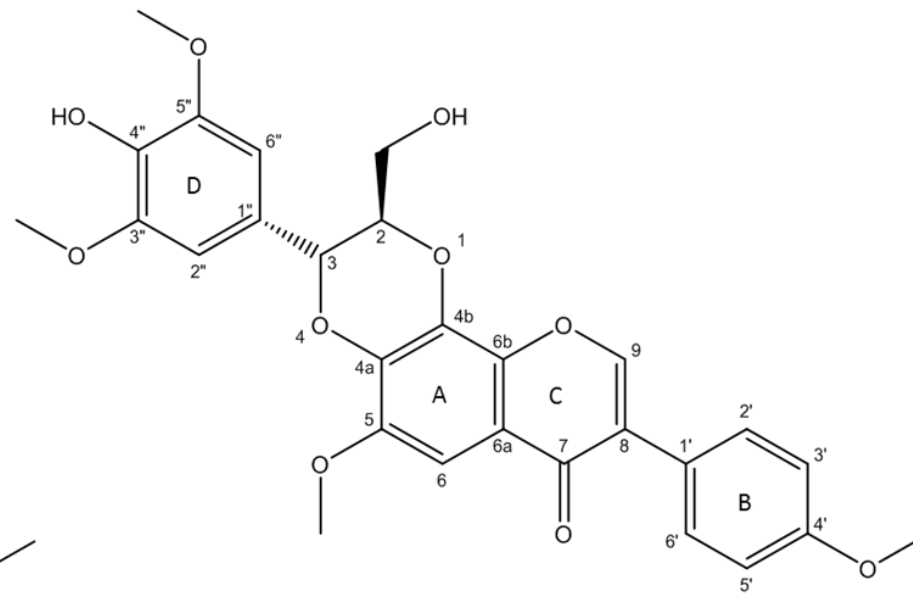


Isolated Active Compounds Through Bioassay-Guided Fractionation and MagMASS with ER α



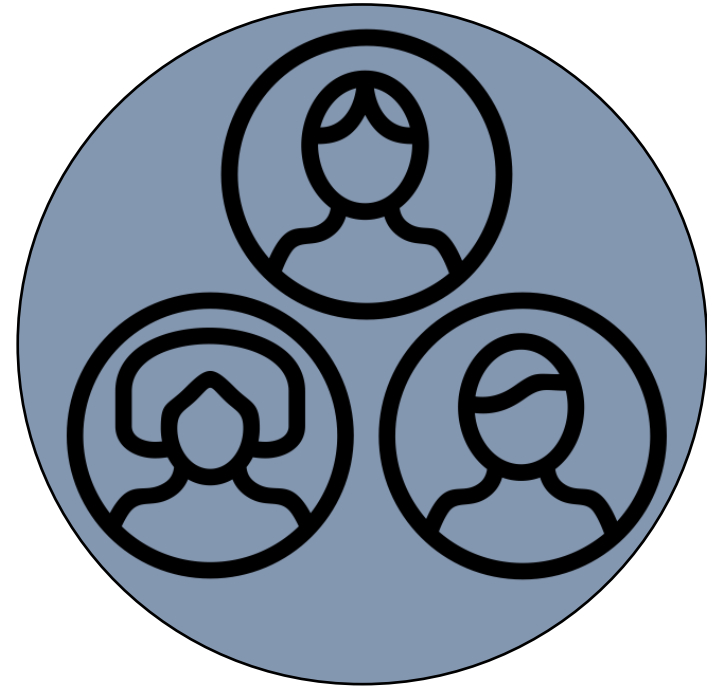


K3: Xanthocerin A



K4: Xanthocerin J

From Benchwork to Community



Aim 2: Ethnobotany

- A. Identify current uses of the tested plants by urban American Indian women
- B. Understand how urban American Indian women perceive and experience menopause

Community Engaged Research with Urban American Indians



Study Design-Focus Groups

- Modified Rapid Ethnographic Assessment (REA)
 - IRB #2016-0840
- Audio-recorded Focus Group
 - Interview Guide
 - Biodemographic Sheet

Interview Guide

As you know, we are mainly interested in having a discussion about menopause and how you treat menopausal symptoms. So I'll ask you some questions about this:

1. When you hear the word menopause, what are your first thoughts?
2. Think about your or someone you know menopausal experience. Tell me about the symptoms and what happened.
3. I am interested in learning about these three plants (pass around picture of the three plants) and their uses for menopausal symptoms and other women's health ailments. Do you know of these three plants?
4. What other plants do you know that we did not mention that are used for menopause or other women's health issues?
5. Based on this conversation, what would you like to see as a future outcome when it comes to American Indian women and their menopausal experience?
6. Is there anything else you would like to add?

Three Focus Groups to Interview Participants

- 32 American Indian Women



American Indian Center of Chicago (previous location),
September 21, 2016



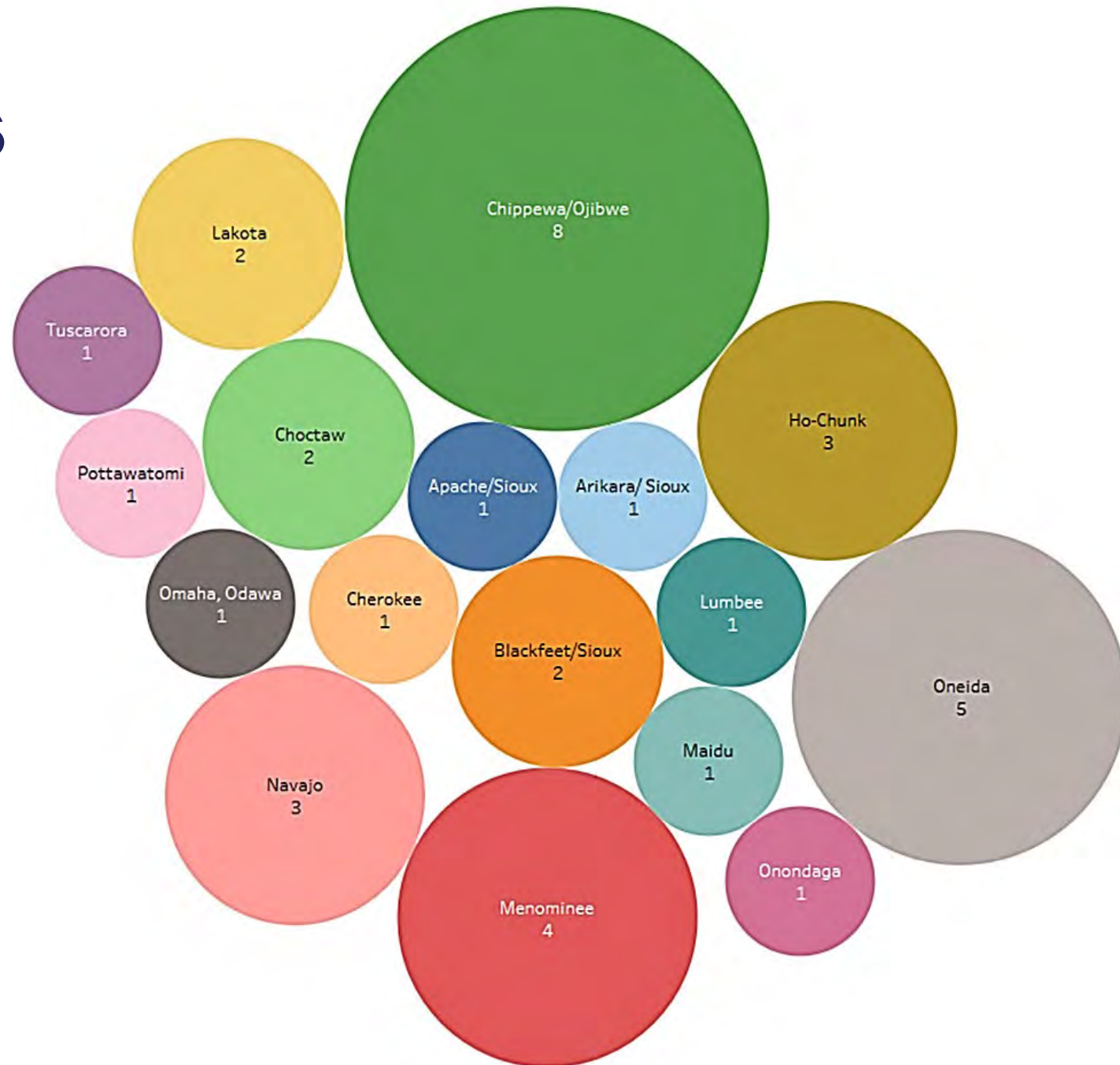
St. Kateri Center of Chicago
September 25, 2016



Wise Women Gathering Place in
Green Bay
November 16, 2016

Demographics

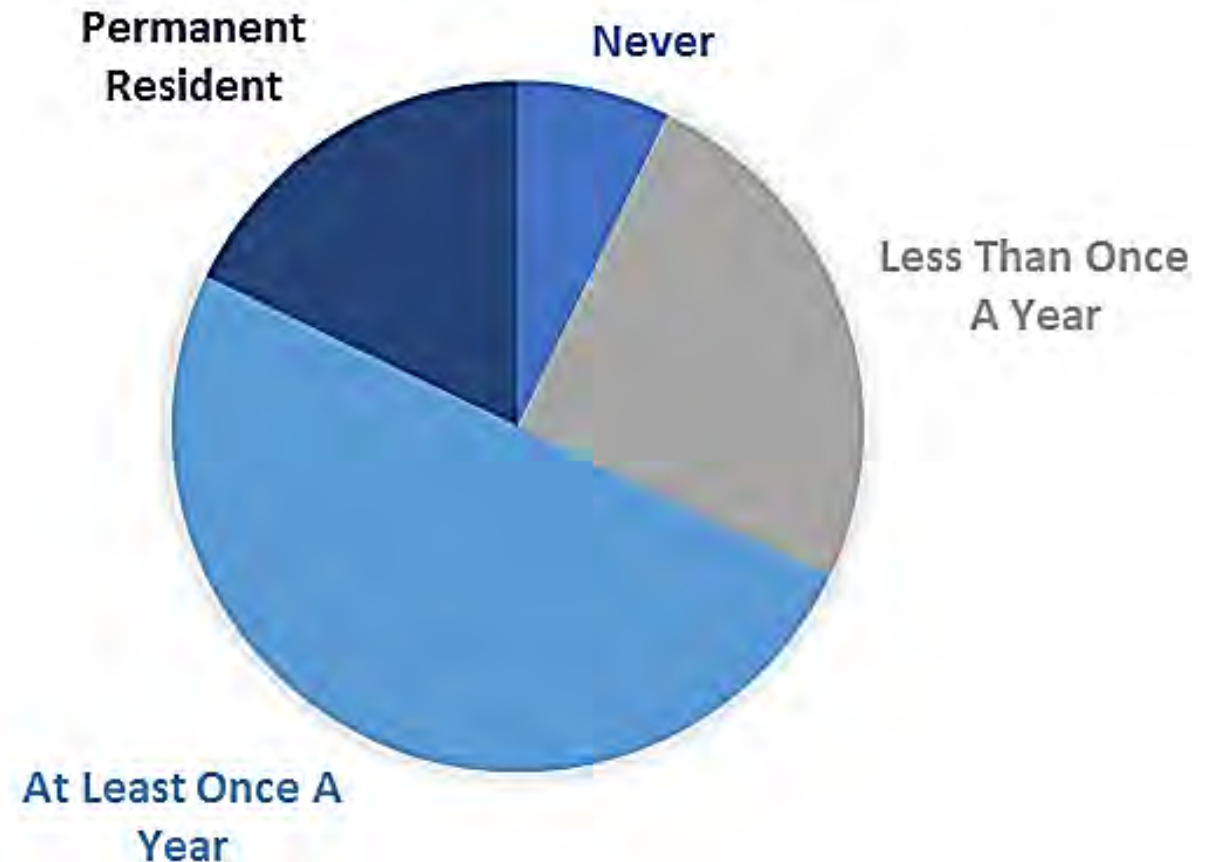
- 32 American Indian Women
- Diverse Tribal Affiliation
 - Represented 17 different home tribes



Demographics

- 32 American Indian Women
- Diverse Tribal Affiliation
 - Represented 17 different home tribes
- Average age of starting menopause ~ 47
- 62% Post-menopausal
- All participants experience menopausal symptoms
- Five women experienced medical treatment

HOME RESERVATION VISITS



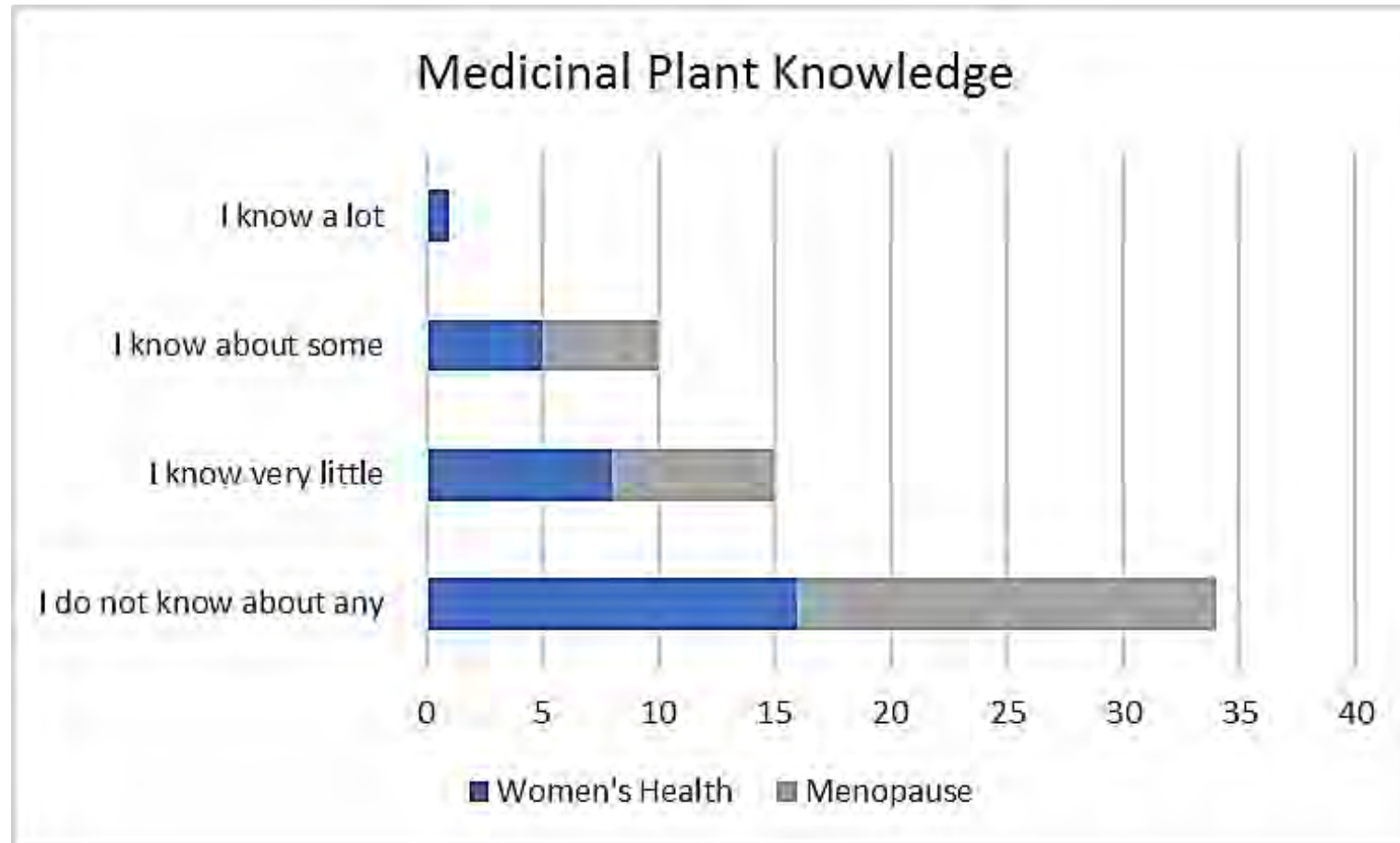
Primary symptoms experienced were hot flashes, difficulty sleeping, night sweats and weight gain

Symptoms	Yes	No	Don't Know
Hot flashes	24	5	0
Difficulty sleeping	21	7	0
Night sweats	19	8	0
Weight gain	18	8	1
Irregular periods	18	9	1
Urinary urgency	16	12	0

Most women interviewed did not treat their symptoms *but* let them pass naturally



Majority ranked their medicinal plant knowledge as “I don’t know about any (plants)”



Investigated plants were not used

BIODEMOGRAPHIC SHEET		FOCUS GROUP
Plant	Use	Plants/Products
Red Raspberry	Menstrual Flow or Irregularities	Cedar Bath
Black Cohosh	Hot Flashes	Red Raspberry leaf tea
<i>Gingko biloba</i>	Night Sweats	Black Cohosh
Black Ash	Decreased Ability to Concentrate	Strawberry teas
Hibiscus	Memory Loss	Cold Sage tea
Tea (<i>Camellia sinensis</i>)	Hot flashes	Soy
Lavender essential oil	Weight Gain	Mint Tea
St. John's Wort	Difficulty sleeping	Chamomile Tea
	Low Mood or Depression	



Menopause Perceptions: Positive, Negative, Indifferent?

Hot flashes

Getting old (laughs).

I can't have children anymore

Um, like miserable. I always think that you know, you're crabby and hot flashes and crazy

I always thought it, before I got, um, got older, I thought it had very negative connotations but due to the media, like commercials and all this stuff, they made you feel like, oh my goodness, this is really ... Life will be over, which I didn't think it was that way at all.

I was happy....No more periods. (laughs). Period. (laughs).

Your circle's almost completed and that you should be happy that you're, you were able to complete this many si- um, this many cycles in your life. Your baby, your youth, your teen, your adult, and then finally your, your senior or elder period. So after she kind of talked with us and explained it like that, for me, just starting to go into it ...

Anxiety

Summary of American Indian Women Perception of Menopause

- Natural process
- Both positive and negative connotations
- Not discussed in American Indian community
- Correlations to menarche (moon)
- Fear at this age

Invisibility of Menopause Recognition

- Many women mentioned that they did not discuss menopause with family or even other women in community
- Only knew about menopause when they started experiencing symptoms

[My] Mother never talked about it, I thought women her age were just nuts

I never talked about it with my mother or grandmother

Don't talk about it because it's too personal

Implementation Items

- Talking Circles
- Menopausal Ceremony
- Discussions across generations and sex about menopause and other health issues
- Indian Health Services involvement (legislative and public policy)
 - Local
 - State
 - National
- Continuation of learning about medicinal plants for women's health

Summary of Ethnobotany Results

- First survey exclusively of urban, intertribal American Indian women on their menopausal perception, symptomology and treatment
- Menopause symptoms are experienced but most women in this study do not treat symptoms
- Hot flashes, difficulty sleeping, and night sweats are the top symptoms experienced
- Interviewed women do not talk about menopause but want to change this by implementing cultural initiatives such as Talking Circles and Menopause Ceremonies



Conclusions

- Holistic approach to scientific research in Pharmacognosy involving American Indian community based participatory research
- Pharmacognostic techniques identified several active plants with traditional uses and characterized one of these plants
- Ethnobotanical techniques identified other medicinal plants for menopause and how urban American Indian women view, experience and treat menopause

Acknowledgements

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- Richard van Breemen
- D. Doel Soejarto
- Birgit Dietz
- Crystal Patil
- CT Che

Women who participated in the Menopause Focus Groups

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