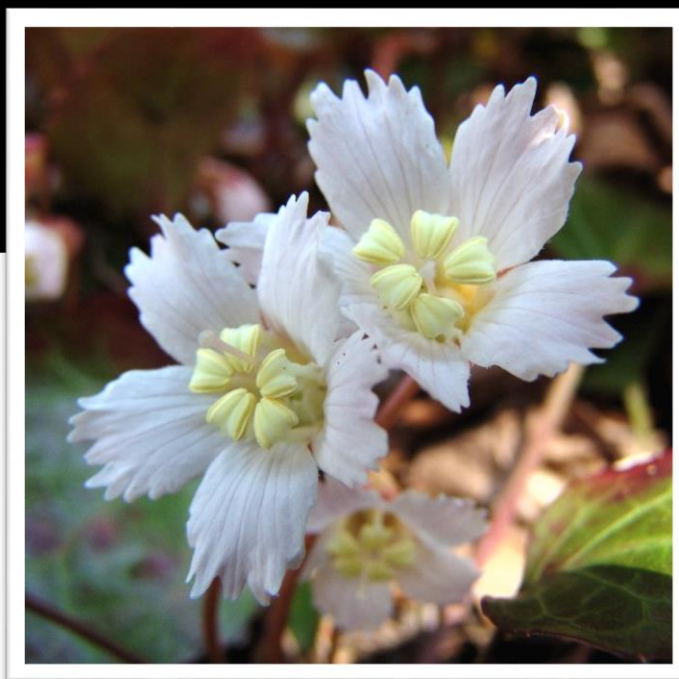


Clemson University Research Foundation Technology Feature:

Natural Anti-tumor Extracts From the Native Plant "Oconee Bell"

CURF ID: 04-001
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Abstract

The **CURF Technology Feature** highlights an emerging technology developed at **Clemson University** which is currently available for licensing. See inside for an introduction to this technology and contact CURF for more information.



Natural Anti-tumor Extracts From the Native Plant “Oconee Bell”

Description:

Although the market for cancer treatment is mature, new treatments are constantly needed to treat or better-target various types of cancer. Minimization or differentiation of side effects, and efficacy at treating early-stage cancers at low doses is also desirable. An increasing segment of the population is also turning to naturally-derived drugs or therapies as preferred treatment strategies.

Two extracts of the Appalachian native plant Oconee Bell, *Shortia galacifolia*, have shown promise in trials designed to predict efficacy in animal systems. These two extracts indicate multiple anti-tumor and anti-mutagen compounds are present within the plant.

In addition to new cancer treatments, these extracts may also have commercial potential as herbal supplements, or cosmetic ingredients, for their cell-protective effects.

Shortia galacifolia (SG) extract performance versus positive inhibitory control: positive inhibitory control camptothecin was “completely effective” at 98.2% tumor inhibition. SG leaf = 69.9%, SG new rhizome = 70.0%, mature rhizome=81.1%.

Applications:

- Source of new anti-tumor drugs (multiple)
- May be sold as herbal extract or supplement
- Adding to cosmetics may increase perceived value within the US (native plant) and elsewhere for its protective effects

Benefits:

- New drugs may produce fewer side-effects, or target particular cancers.
- Multiple drug targets in one plant enhance commercial value.
- Perceived value of natural treatments, including derived drugs, is currently high.

Market:

- High demand for novel cancer treatments in US
- Large segment of population is aging, increasing market potential

Inventors:

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Patent Status:

Patent issued; US Patent No. US7691417 B2

Link to Patent:

<https://www.google.com/patents/US7691417>

Licensing Status:

Available for licensing

CURF Reference:

04-001



The native *Shortia galacifolia* "Oconee Bell"



Current chemotherapy drugs derived from plants



Natural Anti-tumor Extracts From the Native Oconee Bell

Clemson University Research
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Background

- Extract from the native plant Oconee Bell has potential as a naturally-derived anti-tumor pharmaceutical
- Many powerful chemotherapy drugs currently in use are derived from plant sources



The Problem

- New anti-tumor treatments with varying modes of action are always needed to increase patient survival of various cancers
- A wide variety of drugs are needed for cancer treatment to:
 - Target different organs or organ systems
 - Target different stages of cancer progression/ metastasis
 - Avoid specific side effects of chemotherapy, depending on patient needs (e.g. ensure successful pregnancy)
- Consumer demand for naturally-derived and plant-based products has increased rapidly in recent years

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The Invention

**Anti-tumor and anti-mutagenic extract of
Oconee Bell *Shortia galacifolia***

Key Features:

1. Extract from leaf and rhizomes
2. Shown to have anti-tumor effect
3. Shown to have anti-mutagenic effect



Patent Issued:

US # 7,691,417

Oconee Bell is Indigenous to
Southern Appalachians in
NC and SC

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Benefits

- Extract of *S. galacifolia* may prove effective for chemotherapy treatment of human cancers
- Metabolites produced by the plant may have different chemical structure than current treatments, and effectively treat different cancers or produce/mitigate different side-effects
- As a naturally-derived plant product, this treatment may be acceptable to a wide segment of cancer patients
- Because the vegetative portions of the plant are used, extract production may be quicker and more profitable

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Competition

- Many plant-derived chemotherapy drugs are already in use:
 - Topotecan (Brand name: Hycamtin)
 - Approved for ovarian, cervical, and small cell lung cancers.
 - Experimental use for neuroblastoma, Brainstem glioma, Ewing's sarcoma.
 - Etoposide (Brand names: Etopophos, Toposar)
 - Approved for small cell lung and testicular cancers.
 - Teniposide (Brand name: Vumon)
 - Approved for leukemias and lymphomas, especially in children.
 - Docetaxel (Brand names: Taxotere, Docefrez)
 - Approved for head and neck, breast, gastric, and prostate cancers.
 - Paclitaxel (Brand names: Abraxane, Onxol)
 - Approved for AIDS-related Kaposi sarcoma, breast, non-small cell lung, and ovarian cancers.
- All of these drugs are currently being used experimentally to treat additional cancers.

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The Science

Table 1: Tumor inhibition of plant extracts

Potato Tumor Induction			
Sample	Dilution (concentration)	% Tumor Inhibition	Tissue Mean
Control	N/A	0	
LF	1:100 (10 mg/ml)	72.6 ~69.9	
LF	1:1,000 (1 mg/ml)	72	
LF	1:10,000 (0.1 mg/ml)	74.5	
LF	1:100,000 (0.01 mg/ml)	60.6	
NRh	1:100 (10 mg/ml)	86.1 ~70.0	
NRh	1:1,000 (1 mg/ml)	66.4	
NRh	1:10,000 (0.1 mg/ml)	66.7	
NRh	1:100,000 (0.01 mg/ml)	59	
MRh	1:100 (10 mg/ml)	88 ~81.1	
MRh	1:1,000 (1 mg/ml)	81.3	
MRh	1:10,000 (0.1 mg/ml)	78.8	
MRh	1:100,000 (0.01 mg/ml)	79.2	

Potato disc tumor induction assay – “Surprisingly, the plant screening results of the potato disc assay were very strongly associated with the 3PS (*in vivo*, murine leukemia) results ($p=0.002$)...” (McLaughlin et al., 1998)

Table 2: Tumor inhibition for 3 concentrations for solvents and controls

Potato Tumor Induction		
Extraction solvent	Dilution (concentration)	% Inhibition
Hexane	1:100,	63.4
Hexane	1:1,000	27.8
Hexane	1:10,000	17.1
Methanol	1:100,	63.8
Methanol	1:1,000	27
Methanol	1:10,000	5.6
Neg. control (camptothecin)	1:10,000	100

Table 3: Mutation inhibition for extracts from three tissues and control

Ames Salmonella Assay			
Plant Extract	Revertant colonies without 2-AA	Revertant colonies with 3-AA	% Inhibition
Control (DMSO+ S9)	48.2	991.6	N/A
Leaf	50.3	303.3	373
New Growth Rhizomes	48.2	212.9	82.5
Mature Rhizomes	46.2	254	78.2

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Future Development Steps

- Both hexane (non-polar solvent) and methanol (polar solvent) extracts of the plant are effective, indicating that multiple compounds in the plant may be isolated, and that they may have synergistic effects

PRECEDENT: The native plant “May Apple” has produced two chemotherapy drugs (Etoposide and Teniposide), indicating precedent for multiple commercial drugs from one plant source.

- Correlation of initial screenings with efficacy in animal cells may indicate readiness for animal trials
- Extract side-effects might be tested to determine if they differ from current chemotherapy treatments

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US Market for Cancer Treatments:

Market size:

- ~ 11 million new Cancer cases diagnosed each year and approximately 7 million die each year from Cancer. [28]
- by 2020, there will be 16 million new cases, approximately 60% of which will be in developing countries. [29]

Market growth: "Cancer represents the fastest growing therapy segment in the pharmaceutical market. This segment has become the centre of focus for drug firms and investors, and has garnered more attention than any other therapy segment; nearly every mid-size and large pharmaceutical/biotech company today is linked to a cancer pipeline." [3]

Market potential: According to GMR Data's *Cancer Drugs & Treatments Market - Data, Analysis and Forecasts to 2023*, "the global cancer drugs and treatments market will reach **\$143.7bn** by 2023" and is currently estimated at **\$77.4bn** [1]

Major drivers of market:

- Need for Reduced Side Effects [19]
- Aging of the Population [20]
- Increased Cancer Rate in Developing Countries [21] [22]
- Increased Early Detection [23]
- "The US is the largest market for cancer drugs, followed by Europe and Japan." [24]

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Opportunity Summary

Known need and increasing demand

- Cancer is the second most common cause of death in the US¹
- Increasing demand for naturally-derived and plant-based products

Potential Applications

- Source for anti-tumor drugs
- Protective herbal supplements
- Adding to cosmetics



¹- Cancer Facts & Figures. American Cancer Society 2012

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Summary of Benefits

- **Oconee Bell anti-tumor and anti-mutagen extract**
 - May provide **multiple** new drugs for greater investment return
 - May provide organ/tissue-specific cancer treatments
 - May provide different range of side-effects than current cancer treatments
 - May be marketed as a natural or alternative chemotherapy
 - May be marketed as herbal supplement or cosmetics ingredient
- **Attractive Market**
 - High demand for novel cancer treatments in US
 - Large segment of population is aging, increasing market potential
- **Intellectual Property**
 - Patent issued for both extracts (polar and non-polar) of Oconee Bell, from all tissues tested; Link: <https://www.google.com/patents/US7691417>

MORE INFORMATION IS AVAILABLE ABOUT THIS TECHNOLOGY

↳ Access technology specifics at <https://www.google.com/patents/US7691417>

To inquire about this technology or other technologies available for licensing from Clemson University, please contact CURF.

To access an on-demand searchable listing of ***all available technologies*** please visit us online.
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