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(54) **NOVEL BOTANICAL FORMULATION FOR TREATING SICKLE CELL DISEASE**

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(57) **ABSTRACT**

An improved plant medicament composition, comprising an extract of *Sorghum bicolor* plant material for treating sickle cell disease is described. A method for the preparation of said composition having the property of inhibiting sickle cells is also provided.

NOVEL BOTANICAL FORMULATION FOR TREATING SICKLE CELL DISEASE

FIELD OF THE INVENTION

[0001] The present invention relates to the field of botanical formulations, botanical compositions and botanical extracts, particularly as it relates to the phytodrug, prodrug or plant medicament for the treatment and management of sickle cell disease and methods of preparing and using same.

BACKGROUND OF THE INVENTION

[0002] Sickle cell disease (SCD) is a hereditary blood disorder, affecting over 75,000 people in the United States. Sickle cell disease (SCD) affects over twenty million people throughout the world and is particularly common among those whose ancestors come from sub-Saharan Africa, Spanish-speaking regions in the Western Hemisphere (South America, the Caribbean, and Central America), Saudi Arabia, India, and Mediterranean countries such as Turkey, Greece, and Italy.

[0003] In the US, those with SCD have an average mortality in their 40s, a poor quality of life and high medical costs. In SCD, a mutation in β -globin (glu6val) causes deoxygenated sickle hemoglobin (deoxy-HbS) to form insoluble polymers inside red blood cells (RBCs), which deforms the RBCs into rigid shapes or sickle cells that occlude capillaries and small blood vessels. The only disease-modifying drug approved for use in SCD patients is hydroxyurea, an anti-cancer drug. Not all patients respond to hydroxyurea, and it can be poorly tolerated causing myelosuppression in some patients. Despite extensive studies on SCD by researchers over several decades, there has been little progress in the development of additional disease modifying agents. Therefore, new, safer and more effective therapeutic anti-sickling agents are needed to treat patients with SCD, particularly children, which could improve the quality of life, increase the life expectancies of sufferers of this disease, and reduce the estimated 100,000 hospitalizations and \$500 million in direct hospital costs due to sickle cell disease in the United States. Sickle cell disease occurs in about 1 in every 500 African American births, and about 1 in 12 African Americans has sickle cell trait. The morbidity and mortality factors associated with sickle cell disease are well known and the acute and chronic trauma of the painful episodes is indescribable. In view of these realities, there is a desperate need for drugs or agents that could alleviate and mitigate the effects of this terrible disease.

[0004] U.S. Pat. No. 5,800,819 describes a composition requiring extracts from at least four plant materials for treating sickle cell disease. U.S. Pat. No. 5,800,819 does not describe *Sorghum bicolor*, per se, having anti-sickling activity nor measure the anti-sickling activity of *Sorghum bicolor*. It only describes the anti-sickling activity of the four ingredients mixed together. The present invention provides a distinctly different and improved plant formulation using *Sorghum bicolor* plant material, per se, that shows potent anti-sickling activity against human sickle cells and is simpler to formulate.

SUMMARY OF INVENTION

[0005] It is an object of this invention to provide an improved and efficacious botanical medicament for the treatment and management of sickle cell disease.

[0006] It is an additional object of this invention to provide a method for the preparation of an improved plant formulation and preparation for the treatment and management of sickle cell disease.

[0007] Various other objects and advantages of the invention will become obvious from the detailed description of the invention.

DETAILED DESCRIPTION OF THE INVENTION

[0008] Various objects and advantages of the invention are achieved by preparing a botanical formulation comprising an extraction obtained from *Sorghum bicolor* plant, without the use of, or extraction from, any other plant, said extraction from *Sorghum bicolor* plant being effective against sickle cell disease. The *Sorghum bicolor* plant, alone, has not been previously shown to contain anti-sickling activity or anti-sickling compounds. The formulation could be administered in any suitable form such as a tablet, capsule, suspension, solution, powder, and the like, to treat sickle cell disease and may further comprise any pharmaceutically acceptable carrier and excipients well known to a skilled artisan in the field to which this invention belongs.

[0009] A method for preparing a botanical composition, comprises the steps of:

[0010] (i) obtaining an extract having anti-sickling activity from *Sorghum bicolor* plant material; and

[0011] (ii) preparing said extract in a suitable form for treating sickle cells.

[0012] Unless defined otherwise, all technical and scientific terms used herein have the same meaning as commonly understood by one of ordinary skill in the art to which the invention belongs. The term "pharmaceutically acceptable," as used herein, refers to those compounds, materials, compositions, and/or dosage forms which are, within the scope of sound medical judgment, suitable for use in contact with the tissues of patients without excessive toxicity, irritation, allergic response, or other problem or complication commensurate with a reasonable benefit/risk ratio, and are effective for the intended use.

[0013] A typical procedure for extraction using *Sorghum bicolor* plant material is now set forth. *Sorghum bicolor* seeds were grown under normal green house conditions. Canadian pot mixture fortified with anhydrous ferric chloride (10 mg/pot) was used as the growth medium. Watering was done with tap water once a week. Every month the leaves were removed and air-dried. The dried leaves were extracted with aqueous sodium bicarbonate (7.4% concentration W/V at a pH ranging from about 8 to about 8.3) by stirring for about 8 hrs at normal ambient temperature. It should be noted that other buffers or extractants, neutral, organic or inorganic, at different pH could be employed to extract the anti-sickling activity from *Sorghum bicolor*. The extraction process is not limited to sodium bicarbonate or the pH range of 8.0-8.3. The method described herein is only a preferred embodiment of the extraction process. It should also be noted that the manner in which the plant is grown, including but not limited to the soil type, fertility and soil pH may also vary from the method described herein and would influence the amount of anti-sickling activity in the extract obtained from the plant material.

The degree to which plants could vary in the accumulation of natural products that may provide medicinal, therapeutic and biological activity is well known to skilled artisans and the

or manipulations of the present invention would be suggested to a skilled artisan and these are included within the spirit and purview of this application and scope of the appended claims.

TABLE 1

COMPARATIVE RESULTS OF SICKLE CELL BIOASSAY					
Name of sample	Sample ID	Solvent used for concentration at pH 8-8.3	Origin of <i>Sorghum Bicolor</i> seed	Sample description	Bio-Assay (% of cells still sickled)
<i>Sorghum Bicolor</i>	XC-214-41-IS2724	Sod. Bi Carb	India	IS2724 1 month old leaves	23%
<i>Sorghum Bicolor</i>	IS2724-4L	Sod. Bi Carb	India	IS2724 4 month old leaves	38%
<i>Sorghum Bicolor</i>	IS2724-ML-5	Sod. Bi Carb	India	IS2724 5 month old leaves	32%
<i>Sorghum Bicolor</i>	IS2724-IF-4	Sod. Bi Carb	India	IS2724 inflorescent leaves	16%
<i>Sorghum Bicolor</i>	IS2724-SD-5	Sod. Bi Carb	India	IS2724 ground seeds	62%
<i>Sorghum Bicolor</i>	IS2724-ST-5	Sod. Bi Carb	India	IS2724 stem	63%
<i>Sorghum Bicolor</i>	XC-214-41-FF	Sod. Bi Carb	India	Fara Fara 1 month old leaves	36%
<i>Sorghum Bicolor</i>	XC-214-41-Red	Sod. Bi Carb	India	Red Hagari 1 month old leaves	23%
<i>Sorghum Bicolor</i>	PI48771-02-SD	Sod. Bi Carb	South Africa	1 month old green leaves	52%
<i>Sorghum Bicolor</i>	XC-214--38-sb4g	Sod. Bi Carb	South Africa	4 month old green leaves	32%
<i>Sorghum Bicolor</i>	XC-214-42-SA6	Sod. Bi Carb	South Africa	6 month old green leaves	24%
<i>Sorghum Bicolor</i>	PI586787-01-SD	Sod. Bi Carb	Unknown Origin	4 month old green leaves	42%
<i>Sorghum Bicolor</i>	PI513794-01-SD	Sod. Bi Carb	Niger	4 month old green leaves	60%
<i>Sorghum Bicolor</i>	PI155889-0 1-SD	Sod. Bi Carb	Tanzania	4 month old green leaves	64%
<i>Sorghum Bicolor</i>	PI287617-01-SD	Sod. Bi Carb	Zimbabwe	4 month old green leaves	53%
<i>Sorghum Bicolor</i>	PI284971-01-SD	Sod. Bi Carb	Argentina	4 month old green leaves	51%
<i>Sorghum Bicolor</i>	PI810693-01-SD	Sod. Bi Carb	China	4 month old green leaves	54%
<i>Sorghum Bicolor</i>	PI585454-01-SD	Sod. Bi Carb	Ghana	4 month old green leaves	28%
<i>Sorghum Bicolor</i>	XC-214-41-Nunba	Sod. Bi Carb	Nigeria	Nunaba, 1 month old leaves	24%
<i>Sorghum Bicolor</i>	XC-214-41-Nig2	Sod. Bi Carb	Nigeria	2 month old green leaves	16%
<i>Sorghum Bicolor</i>	XC-214-41-Nig6	Sod. Bi Carb	Nigeria	6 month old green leaves	26%
Nicosan	U.S. Pat. No. 5,800,819	Potash	Nigeria	Nicosan from Nigeria	88%
Control-Buffer	Ctr		500	0	97%
Control-Buffer	Ctr		500	0	98%

ability to standardize the extract to ensure pharmacologically efficacious activity by any suitable method is included in this invention, the bioassay described herein being only an example.

[0014] The extract was allowed to settle, and then decanted, filtered, centrifuged and freeze-dried.

[0015] The freeze-dried material was thoroughly blended to form a uniform mixture, which could be formulated in any suitable form, such as tablets, granules, capsules, suspensions, solutions, and the like, by well known methods. Buffers, emollients, additives, supplements, preservatives, inactive ingredients, fillers, and the like, well known to one of ordinary skill in the art to which this invention belongs, could be added to any formulation prepared by using the *Sorghum bicolor* extract.

[0016] Chemical analyses of extracts from several *Sorghum bicolor* varieties obtained from various sources were carried out using HPLC. The sickle cell bioassay was carried out by using blood removed from a sickle cell subject and exposed to the extract in vitro to measure antisickling activity employing counting and imaging techniques as described in Iyamu, et al, *British Journal of Hematology*, (2002), 118: 337-343.

[0017] The results shown in Table 1 indicate that *Sorghum bicolor* extract, without using plant material from any other source, has potent antisickling activity, having as much as five-fold greater anti-sickling efficacy against human sickle cells, compared to the prior art formulation disclosed in U.S. Pat. No. 5,800,819.

[0018] It should be noted that the guidance, illustrations and examples provided herein are only illustrative and not limiting, and various alternate embodiments, modifications

1. A botanical composition for inhibiting sickling in sickle cell disease, comprising an extraction from *Sorghum bicolor* plant material, without using material from any other plant, said extraction being effective against sickle cells.

2. The composition of claim 1 further comprising any pharmaceutically acceptable carrier and excipients.

3. The composition of claim 2, wherein said extraction is formulated as a solution, suspension, powder, tablet or capsule.

4. A method for preparing a botanical composition, comprising the steps of:

- (i) obtaining an extract having anti-sickling activity from *Sorghum bicolor* plant material; and
- (ii) preparing said extract in a suitable form for treating sickle cells.

5. The method of claim 4, comprising the steps of:

- (i) extracting *Sorghum bicolor* plant material with a 7.4% weight by volume aqueous solution of sodium bicarbonate at a pH ranging from about 8.0 to about 8.3 by stirring for about 8 hr at normal ambient temperature;
- (ii) allowing the extract to settle, then decanting, filtering, centrifuging and freeze drying the resulting material; and
- (iii) thoroughly blending the freeze dried material to form a uniform mixture.

6. The method of claim 5, further comprising any pharmaceutically acceptable carrier and excipients.

7. The method of claim 6, administering said blended uniform mixture for treating sickle cell disease in a powder, tablet, capsule, granular or suspension form.