Medicinal plants used in the treatment of sickle cell disease in Western Africa

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Abstract

Sickle cell disease is a serious problem in Africa where the required medication is often not available or too expensive for local Africans. Other possibilities have to be investigated, like traditional medication in the form of medicinal plants to control the symptoms of the disease. By screening scientific articles, a big table in Excel was made, containing 93 species which all have a potential effect against sickle cell disease. *Cajanus cajan*, *Carica papaya*, *Piper guineense*, *Pterocarpus osun*, *Sorghum bicolor*, *Syzygium aromaticum*, *Zanthoxylum zanthoxyloides*, *Justicia secunda*, *Moringa oleifera* and *Vinga unguiculata* seem to be the most promising species for treatment. To solve the problem of unaffordable medication, a closer look should be taken to the common food crops in the table which have a possible effect against sickle cell disease.

Introduction

Sickle cell disease (SCD), also known as drepanocytosis, is a genetic blood disorder in which red blood cells form an abnormal sickle or crescent shape. This genetic disease is due to a mutation in the β-globin gene in which the 17th nucleotide is changed from thymine to adenine and the sixth amino acid in the β-globin chain of hemoglobin whereby glutamic acid, a polar amino acid, is replaced by valine, a non-polar amino acid. This mutation decreases the affinity of hemoglobin for oxygen. At low oxygen tension the mutant hemoglobin, called hemoglobin S, polymerizes inside the red blood cells leading to a severe decrease in the red cell deformability. Polymerization and precipitation of hemoglobin S within the red blood cells cause the change of their shape from their normal disc-like form into one resembling a sickle (Mehanna, 2001; Bender, 1993; Rees, 2010). In Figure 1, part A shows normal red blood cells flowing freely in a blood vessel. The inset image shows a cross-section of a normal red blood cell with normal hemoglobin. Part B shows abnormal, sickled red blood cells blocking blood flow in a blood vessel. The inset image shows a cross-section of a sickle cell with abnormal hemoglobin forming abnormal strands. (http://www.nhlbi.nih.gov/health/health-topics/topics/sca/)
The symptoms which are caused by the sickle shaped cells are due to a shortage of good functioning blood cells, which causes anemia, blood clotting and blockage of blood vessels. They vary from fatigue, to dizziness and headaches, during a mild sickle cell crisis. A drastic sickle cell crisis is an acute episode of severe pain. These crises occur when sickled red blood cells block the blood flow to the limbs and organs, which causes the pain and eventually irreversible organ damage (Steinberg, 1999; Bender, 1993).

SCD cannot be cured, so the goal of treatment is to manage and control symptoms, and to limit the number of crises (www.nhlbi.nih.gov). Patients with SCD need continuous treatment, even when they are not experiencing a painful crisis. The treatment includes pain medicines, fluids for hydration, blood transfusion to replace the sickled cells, multiple vaccines and antibiotics. The last two are necessary because of acute splenic sequestration, which occurs mostly in young patients. Sickle cells clump inside the spleen, which then becomes enlarged and cannot function properly anymore. This makes the patients more viable for infections and needy of the vaccines and antibiotics (Emond et al., 1985). In a crisis situation, multiple operations may be necessary for the transplantation of damaged organs. Also a bone marrow transplant can be performed, where the bone marrow stem cells are replaced by those of a donor and the newly made red blood will not form into a sickled shape (http://www.hematologienederland.nl/sikkelcelziekte).
The problem
Sickle cell disease is prevalent in tropical Africa. In Northern and Southern Africa, 1-2% of the population is a carrier of the disease, a heterozygote. In countries such as Congo, Gabon, Benin, Ghana and Nigeria this percentage reaches up to 20-30%. The geographic distribution of the sickle cell trait is similar to that of malaria. This is because heterozygotes actually have an advantage, above people without SCD, as they are protected against the severe form of malaria. Consequence is that people who are heterozygous reach maturity more often than those who are not. In countries, where the percentage of carriers is higher than 20%, about 2% of the population is born with SCD, the homozygotes (http://www.afro.who.int).

The required medication to treat SCD is often not readily available to most rural Africans, especially in the poorest countries. They cannot afford the available treatments, as they always need continuous medication, because SCD cannot be cured, only controlled. In Congo for example, where the average daily wage is less than 1 US dollar, people cannot afford the cheapest available haemoglobin S test, which is about 2.5 US dollars (Tshilolo et al., 2009). Buying this test means they cannot eat for one or probably more days, and the treatments are not even included yet. All these factors make SCD a large problem in Africa which should be taken seriously.

Because of the expensive tests, medication and treatments, rural Africans often rely on traditional medicine to treat this disease, which comes in the form of plant extracts. It is not clear though, which plant species actually have an positive effect on the sickled cells or the symptoms of SCD and may function as a treatment for the disease. Experiments have been done on several African plant species to evaluate their effect against SCD, but no clear overview exists about which species have been tested and actually have a proven effect.

Aim of the research
The aim of this research is to review which plant species are being used in Africa for the treatment of SCD, and which of those are promising species to effectively treat this disease. This is very important to determine, as African people who suffer from SCD may benefit greatly from further testing of these species. Using effective medicinal plants can be an affordable way for them to treat the symptoms of SCD and cope with the disease.

Main- and sub research questions
Which plants are used to treat sickle cell anemia in Western Africa?

1. Have these plants been studied pharmacologically for their potential to treat sickle cell disease related ailments?
2. Which plants have a potential to reduce sickle cell anemia related health problems?
3. How do Africans view the cause and treatment of sickle cell disease?
Method
The first step of this research was to search for scientific articles in Google scholar (http://scholar.google.nl/) and Pubmed (http://www.ncbi.nlm.nih.gov/pubmed) about the treatment of sickle cell disease in Africa by plants, and make a clear summary of the results described in these papers. I used the search terms ‘drepanocytose’ and ‘sickle cell’ in combination with the terms ‘disease’, ‘anemia’, ‘Africa’, ‘plants’, ‘herbs’, ‘traditional medicine’, ‘medicinal plants’, ‘anti-sickling’ and ‘anthocyanins’.

In order to do this I made an Excel table, containing the collected plant species, family, countries where the species was used in to treat SCD, whether the species had an anti-sickling effect of the red blood cells according to the article, if the anti-sickling or other mentioned effects of the species were proven by means of an in vivo or in vitro test and the active principle in the plant which according to authors, was responsible for the anti-sickling effect.

Since many Africans think the colour of the plant affects its effectiveness, they believe that red plant medicines will cure red blood (Cocks et al., 2002). Therefore, I noted whether any part of the plant (roots, stem, leaves, fruit, flowers) had a red, pink or purple colour. This information was acquired from literature or by typing in the species in www.google.com and then clicking ‘Images’, or from images from www.wikipedia.com. Species names were updated by using The Plant List (www.theplantlist.org).

I also collected information from unpublished plant use databases from Ghana by postdoc researcher Tinde van Andel, from Benin and Gabon by PhD Candidate Alexandra Towns and from Julie-Anne Borm. Julie-Anne has been a project leader of the Association of Cooperating Parent and Patient Organizations (‘Vereniging van Samenwerkende Ouder- en Patiëntenorganisaties’, VSOP) in the Netherlands. When I listed a species from these databases, I mentioned it in the references as ‘Unpublished’, together with the name of the person of my source.
I retrieved all the information in the excel table from the articles, except the tabs ‘Family’, ‘Genus and Species THEPLANTLIST.ORG’ and ‘Red colour’. I got the information of the first two tabs from www.theplantlist.org.

I held an interview with Julie-Anne Borm, who is knowledgeable on SCD and who could tell me her field experiences about African people that use plants in order to treat this disease. This I did to have a better understanding in the thoughts of Africans related to SCD.

Results
Plant species used against SCD
About 40 articles were reviewed and screened for information about plants that were used traditionally against SCD. A total of 93 species was found, from 49 different families (see appendix). The best represented families, containing 5 species or more, were the Leguminosae (12), Apocynaceae (6), Rubiaceae (5), Euphorbiaceae (5) and Annonaceae (5). This is not really a surprise as they all belong to the major group Angiosperms which has over 5.000 accepted species’ names (www.theplantlist.org). From the 93 species, a total of 54 species had been proven to work against SCD, which was 58% of the total. Almost all of these tests on these plants were done ‘in vitro’, which means the biological technique was performed in a lab in a test tube, instead of in a living creature. This mostly worked by starting to
take blood samples from adolescent subjects with SCD. The blood was screened first to check if they actually had SCD and they obtained dried and powdered plant material from the species they wanted to test. The blood samples were put in contact with the plant extracts at different concentrations. It was put together on a glass slide, and under the microscope checked for a possible anti-sickling effect (Mpiana et al., 2007).

**Active principles**
Of the 54 species studied for their possible effect, active principles were identified for 27 species (50%). In 21 of these cases, anthocyanins seemed to be responsible for the anti-sickling effect. Anthocyanins are natural colorants belonging to the flavonoid family. They are commonly distributed among flowers, fruits, and vegetables. Additionally to their colorful characteristics, they have potent antioxidant properties. This makes them have an array of health-promoting benefits, as they can protect against a variety of oxidants through a various number of mechanisms. They are found in all plant tissues throughout the plant kingdom, but come in many forms which can have different properties (Wang et al., 1997; Kong et al., 2003).

**Red colour**
From the total of 93 species found, 48 (51.6%) seemed to have red parts in either their roots, stem, leaves, fruit, or flowers. Out of the 54 species that had been proven to work, 32 (59.2%) have a red organ. There does not seem to be a direct relation between red plants, and a possible effect against SCD. It could be that local Africans prefer to use red plants as they believe the colour of the plant affects its effectiveness, but as only slightly more than half of the species in the table have red parts, this statement cannot be proven.

To determine which plant species were the most promising to have an effect against SCD, I first looked at the species which were cited most often in articles (See Table 1).

**Table 1. Plant species used against SCD cited in more than three papers**

<table>
<thead>
<tr>
<th>Species</th>
<th>Number of articles</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cajanus cajan</td>
<td>4</td>
</tr>
<tr>
<td>Carica papaya</td>
<td>4</td>
</tr>
<tr>
<td>Piper guineense</td>
<td>3</td>
</tr>
<tr>
<td>Pterocarpus osun</td>
<td>3</td>
</tr>
<tr>
<td>Sorghum bicolor</td>
<td>4</td>
</tr>
<tr>
<td>Syzygium aromaticum</td>
<td>3</td>
</tr>
<tr>
<td>Zanthoxylum zanthoxyloides</td>
<td>4</td>
</tr>
</tbody>
</table>

The plants listed in table 1 all have a proven anti-sickling effect against SCD. *Pterocarpus osun* is part of the SCD medicine Niprisan, or renamed Nicosan. This medicine is a product of the extracts of four different kinds of plants: the seeds of *Piper guineense*, the fruit of *Eugenia caryophyllum*, the leaves of *Sorghum bicolor* and the stems of *Pterocapus osun*. The herbal medicine has been used locally among folk groups in Nigeria to prevent painful crises that are associated with SCD, and seems to have a strong
anti-sickling effect. Although the medicine worked, Nicosan was not really a success. (Iyamu et al., 2002). There are more promising species, like *Justicia secunda*, *Moringa oleifera*, and *Vinga unguiculata*, which are currently investigated in Congo to be combined to generate a new medicine to control SCD (Borm, personal communication).

**The African view**

African people who are confronted with SCD, either because family members or they themselves have the disease, are most of the time not familiar with or well informed on the disease. Many Africans believe SCD is caused by a curse from enemies, the work of “Satan” or other supernatural (witchcraft) factors (Ohaeri et al., 2001). There is also a disease named ‘La rate’ by locals, which looks very familiar to a symptom of SCD, splenic sequestration (Towns, personal communication). This is a spleen crisis in which sickled cells block the blood vessels leading out of the spleen, so that the blood stays inside. The spleen gets very large because of the accumulation of blood, and can feel painful. La rate is described as a swelling and pain on the left side of the body, and most of the time, just like splenic sequestration, diagnosed with children. It could be very possible that la rate is actually a symptom of SCD instead of a disease itself.

**Discussion**

Unfortunately, there are some gaps present in the table (see appendix). In some of the articles, it was not clear in which countries the plant species were used, active principles were not mentioned, or the colour of the plant was not to find out.

Furthermore, as earlier mentioned, could the disease la rate be a symptom of SCD. However, this is still just a thought and has never been proven. It could be that la rate is actually something very different from SCD. In that case, the species in the table with ‘La rate’ in the tab ‘Other information’, should be excluded from the table. More investigation should be done on la rate in Africa, to found out if this disease is indeed a sign of SCD.

A lot of species, 36.3% to be exact, are from the author P.T. Mpiana. He is a professor at the University of Kinshasa in Congo (http://www.unikin.cd/index.php?page=pub-chimie) and has spent the last twenty years on studying medicinal plants on their effectiveness against SCD and publishing the results. It seems not very reliable if a lot of plant species in the table are only tested, and been proved to have an anti-sickling effect by only one author. Fortunately, a part of the plant species in Mpiana’s articles are also mentioned in other articles, but this situation states that more investigation should to be done on all of these plants and their anti-sickling effect.

Additionally, I think best would be to test these plants in vivo instead of only in vitro, so the results and conclusions are better related to real SCD in people. The problem is, that there is very little funding available for research, especially for neglected diseases like SCD. Also, barriers are faced in translating traditional medicinal knowledge into commercially viable health products. For example insufficient manufacturing capacity, quality control issues and pricing and distribution (Perampaladas et al., 2010).
Finally, I already mentioned that the red colour of the plants could not be proven to have an effect on SCD. It could be possible, that the red plants in fact have a placebo effect on the local Africans instead of being really effective. For example when the plants are red, the same colour as blood, they have the idea the plants can cure their blood. I mention this again because some of the red species proven in the table are the outcome of questionnaires, and may not be very reliable.

**Conclusion**

According to my research, the following species are the most promising to have a potential to reduce sickle cell anemia related health problems: *Cajanus cajan, Carica papaya, Piper guineense, Pterocarpus osun, Sorghum bicolor, Syzygium aromaticum, Zanthoxylum zanthoxyloides, Justicia secunda, Moringa oleifera* and *Vinga unguiculata*.

I think definitely more research is needed on these plants and also on other species in the table which seemed to have a proved effect against SCD.

However, if in time all these plants are investigated and new medication can be produced, there are still local Africans who will never be able to afford the medicines. What I think would be best is to promote anti-SCD plants as food instead of expensive medicines. Because when you look at the species registered in the table, a lot of them are actually very common food crops. In the tab ‘Genus and Species PLANTLIST.ORG’, I marked the common food crops with a ‘*’.* The common food crops with a proven anti-sickling effect, I marked with a ‘**’.* There are actually nine species with one asterisk, and nine more species with two asterisks. These are crops, fruits, herbs or spices, that people can simply buy on a market or even grow on their own land. If more health education is given on SCD and the locals are being told about these species, they may benefit and control the SCD symptoms by eating these plant species on daily basis.

**Acknowledgements**

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**References**

**Articles**


Okpuzor, J., Adebesin, O., 2006. Membrane stabilizing effect and antisickling activity of *Senna podocarpa* and *Senna alata*. 31st congress for European biochemical societies, Instanbul, Turkey.


Links
- http://google.com
- http://scholar.google.nl/
- http://theplantlist.org
- http://wikipedia.com

http://www.hematologienederland.nl/sikkelcelziekte


http://www.nhlbi.nih.gov/health/health-topics/topics/sca/

http://www.nhlbi.nih.gov/health/health-topics/topics/sca/signs.html