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PLANTS TO TREAT SICKLE CELL DISEASE

1 Sickle cell disease

In a hereditary disease the reason for being sick is in the genes that everyone is getting from both parents. For each gene we have one from our father and one from our mother.

In sickle cell disease both parents have one healthy gene and one sickle cell gene. With every pregnancy the risk to have a child with sickle cell disease is 1 out of 4 (25%); in 50% (2 of 4) the baby will be a carrier like the parents with one healthy and one sick gene; in 1 of 4 (25%) there is a chance to have a healthy child with 2 normal genes.

Sickle cell disease is a hereditary disease

- **A = healthy gene**
- **S = sickle cell gene**
- **AS** parents have a healthy and a sick gene, they are carriers without symptoms

chance of their children

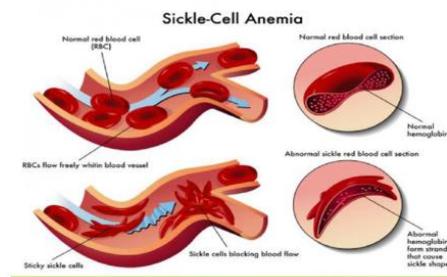
- 25% healthy
- 50% carriers without symptoms
- 25% sickle cell disease present

Normal red blood cells are round and smooth; they can enter the small blood vessels to give the oxygen to the cells of our body.

In sickle cell disease the red blood cells change the shape in certain conditions; they change into the shape of sickles and block small arteries in the body. This can affect all organs; the main organ is the spleen which is an important organ for our immunity and fights infections.

Sickle form of red blood cells leads to:

- Block of small vessels with painful crisis in
 - spleen
 - bones
 - lungs
 - kidneys
 - bowel
 - heart
 - brain
- Anaemia
- Infections



Infections are much more dangerous for sickle cell patients than for a normal person. Sickle cell crises are very painful and chronic bone pain is a common symptom in the disease.

Sickle cell disease is also known as sickle cell anemia, hemoglobin S or SS disease, sickling disorder due to hemoglobin S.

More detailed information

To add more information about the disease the following is copied from different websites <https://www.nhlbi.nih.gov/health-topics/sickle-cell-disease> National Heart, Lung and Blood Institute, National Institute of Health, US Department of Health and Human Services:

Sickle cell disease is a group of inherited red blood cell disorders that affects hemoglobin, the protein that carries oxygen through the body. Normally, red blood cells are disc shaped and flexible to move easily through the blood vessels. If you have sickle cell disease, your red blood cells are crescent or “sickle” shaped. These cells do not bend and move easily and can block blood flow to the rest of your body.

The blocked blood flow through the body can lead to serious problems, including stroke, eye problems, infections and episodes of pain, called pain crises.

Sickle cell disease is a lifelong illness. A blood and bone marrow transplant is currently the only cure for sickle cell disease. But there are effective treatments that can reduce symptoms and prolong life.

People who have sickle cell disease have abnormal hemoglobin, called hemoglobin S or sickle hemoglobin, in their [red blood cells](#). Hemoglobin is a protein in red blood cells that carries [oxygen](#) throughout the body. People who have sickle cell disease inherit two abnormal hemoglobin [genes](#), one from each parent.

1.1 Hemoglobin S gene

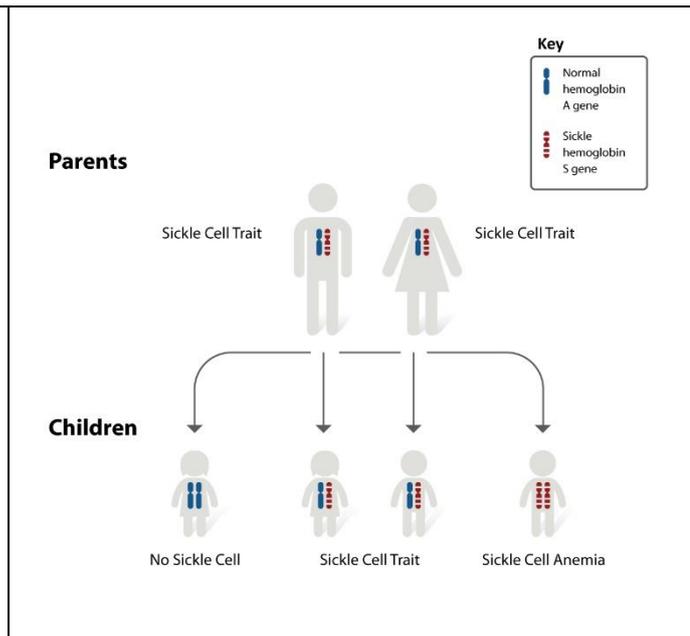
Sickle cell disease is an [inherited](#) disease caused by defects, called [mutations](#), in the beta globin gene that helps make hemoglobin. Normally, hemoglobin in red blood cells takes up oxygen in the lungs and carries it through the arteries to all the cells in the tissues of the body. Sickle hemoglobin is not like normal hemoglobin. The mutations in the gene cause a problem when oxygen levels in the blood are lower, which occurs once the hemoglobin has delivered oxygen to the cells in the body’s tissues. With less oxygen, the abnormal hemoglobin S gene can cause rigid, non-liquid protein strands to form within the red blood cell. These rigid strands can change the shape of the cell, causing the sickled red blood cell that gives the disease its name.

Sickle-shaped cells are not flexible and can stick to vessel walls, causing a blockage that slows or stops the flow of blood. When this happens, oxygen is unable to reach nearby tissues. The lack of oxygen in tissue can cause attacks of sudden severe pain, called pain crises. These pain attacks can occur without warning, and a person who has them often needs to go to the hospital for effective treatment.

Because sickle cells cannot change shape easily, they tend to burst apart. Normal red blood cells live about 90 to 120 days, but sickle cells last only 10 to 20 days. The body is always making new red blood cells to replace the old cells. However, in sickle cell disease, the body may have trouble keeping up with how fast the cells are being destroyed. Because of this, the number of red blood cells is usually lower than normal. This condition, called [anemia](#), can cause a person to have less energy.

1.1.1 How is the hemoglobin S gene inherited?

When the hemoglobin S gene is inherited from only one parent, and a normal hemoglobin gene—hemoglobin A—is inherited from the other, that person will have sickle cell trait. People who have sickle cell trait are generally healthy. Only rarely do people who have sickle cell trait have complications similar to those seen in people who have sickle cell disease. But people who have sickle cell trait are carriers of a defective hemoglobin S gene, so they can pass it on when they have a child.



1.1.2 Signs, symptoms, complications, diagnosis and treatment

If a person has sickle cell disease, it is present at birth. But most newborns do not have any problems from the disease until they are about 5 or 6 months of age.

The symptoms of sickle cell disease can vary from person to person and can change over time. Over time, you may experience symptoms depending on how sickle cell disease affects your health.

1.1.2.1 Early signs and symptoms

Early symptoms of sickle cell disease may include:

- A yellowish color of the skin, known as jaundice, or whites of the eyes, known as icterus, that occurs when a large number of red cells undergo [hemolysis](#)
- [Fatigue](#) or fussiness from anemia
- Painful swelling of the hands and feet, known as [dactylitis](#)

1.1.2.2 Complications

Complications of sickle cell disease include:

- **Acute chest syndrome.** Sickling in blood vessels of the lungs can deprive lungs of oxygen. This can damage lung tissue and cause chest pain, fever, and difficulty breathing. Acute chest syndrome is a medical emergency.
- **Acute pain crisis.** Also known as sickle cell or vaso-occlusive crisis, this can happen without warning when sickle cells block blood flow. People describe this pain as sharp, intense, stabbing, or throbbing. Pain can strike almost anywhere in the body and in more than one spot at a time. Common areas affected by pain include the abdomen, chest, lower back, or arms and legs. A crisis can be brought on by high altitudes, dehydration, illness, stress, or temperature changes. Often a person does not know what triggers the crisis.

- **Chronic pain.** Chronic pain is common, but it can be difficult to describe, but it is usually different from crisis pain or the pain that results from organ damage.
- **Delayed growth and puberty.** Children who have sickle cell disease may grow and develop more slowly than their peers because of anemia. They will reach full sexual maturity, but this may be delayed.
- **Eye problems.** Sickle cell disease can injure blood vessels in the eye, most often in the retina. Blood vessels in the retina can overgrow, get blocked, or bleed. This can cause the retina to detach, which means it is lifted or pulled from its normal position. These problems can lead to vision loss.
- **Gallstones.** When red blood cells break down, in a process called hemolysis, they release hemoglobin. Hemoglobin then gets broken down into a substance called bilirubin. Bilirubin can form stones, called gallstones that get stuck in the gallbladder. The gallbladder is a small sac-shaped organ beneath the liver that helps with digestion.
- **Heart problems,** including coronary heart disease and pulmonary hypertension. Frequent blood transfusions may also cause heart damage from iron overload.
- **Infections.** The spleen is important for protection against certain kinds of infections. If you have sickle cell disease, a damaged spleen raises the risk for certain infections, including chlamydia, haemophilus influenzae type B, salmonella, and staphylococcus.
- **Joint problems.** Sickling in the hip bones and, less commonly, the shoulder joints, knees, and ankles, can decrease oxygen flow and result in a condition called avascular or aseptic necrosis, which severely damages the joints. Symptoms include pain and problems with walking and joint movement. Over time, you may need pain medicines, surgery, or joint replacement.
- **Kidney problems.** Sickle cell disease may cause the kidneys to have trouble making the urine as concentrated as it should be. This may lead to a need to urinate often and to bedwetting or uncontrolled urination during the night. This often starts in childhood.
- **Leg ulcers.** Sickle cell ulcers are sores that usually start small and then get larger and larger. Some ulcers will heal quickly, but others may not heal and may last for long periods of time. Some ulcers come back after healing. People who have sickle cell disease usually do not get ulcers until after age 10.
- **Liver problems.** Sickle cell intrahepatic cholestasis is an uncommon but severe type of liver damage that happens when sickled red cells block blood vessels in the liver. This blockage prevents enough oxygen from reaching liver tissue. These episodes are usually sudden and may happen more than once. Children often recover, but some adults may have chronic problems that lead to liver failure. Frequent blood transfusions can lead to liver damage from iron overload.
- **Pregnancy problems.** Pregnancy can increase the risk for high blood pressure and blood clots in women who have sickle cell disease. The condition also increases the risk of miscarriage, premature birth, and low birth weight babies.

- **Priapism.** Priapism is an unwanted, sometimes prolonged, painful erection. This happens when blood flow out of the erect penis is blocked by sickled cells. Over time, priapism can cause permanent damage to the penis and lead to impotence. Priapism that lasts for more than 4 hours is a medical emergency.
- **Severe anemia.** People who have sickle cell disease usually have mild to moderate anemia. At times, however, they can have severe anemia, which is life-threatening.
- **Stroke or silent brain injury.** Silent brain injury, also called silent stroke, is damage to the brain without showing outward signs of stroke. This injury is common and can be detected on magnetic resonance imaging (MRI) scans. Silent brain injury can lead to difficulty in learning, making decisions, or holding down a job.

1.1.2.3 Diagnosis

Your doctor may use a number of tests to diagnose sickle cell disease if various screening tests show that you might have the condition.

1.1.2.4 Treatment

A [blood and bone marrow transplant](#) is currently the only cure for some patients who have sickle cell disease. After early diagnosis, your doctor may recommend medicines or transfusions to manage complications, including chronic pain.

Copied from healthresearchfunding.org

Approximately 5% of the world's population carries trait genes for hemoglobin disorders. 25% of people in western and central Africa that are believed to have the sickle cell trait. 500,000 babies around the world are believed to be affected by this disease in some way every year.

The number of sickle cell anemia cases is expected to increase about 30% globally by 2050. Up to 90% of the children in developing countries will die in their first 5 years of life because of a lack of treatment options.

In Nigeria, an estimated 91,000 babies are born with the disorder each year. In the Congo about 40,000 babies every year who will be born with this disease.

Copied from *ICMR (Indian Council of Medical Research)*:

About 20 % of children with sickle disease in India died by the age of two as reported in one ICMR survey, and 30 % children with SCD among the tribal community die before they reach adulthood.

1.2 Sickle cell and Malaria

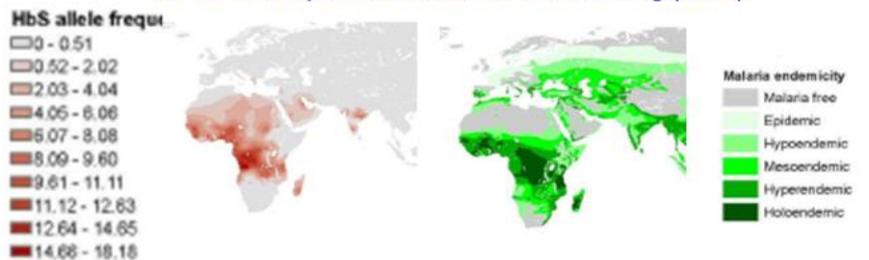
The disease is seen in areas where there is also malaria. People with one sickle cell gene and one normal gene are protected against malaria. In the slide it can be seen that malaria and sickle cell disease are present in the same areas of the world.

Carriers with only one sickle gen are protected against malaria

this experience is confirmed by Malaria Atlas Project (Lit.1)

Sickle cell disease is present only in areas where carriers experience a survival benefit because they are protected from malaria.

For sickle cell patients malaria is life threatening (Lit 13)



Global distribution of sickle cell gene

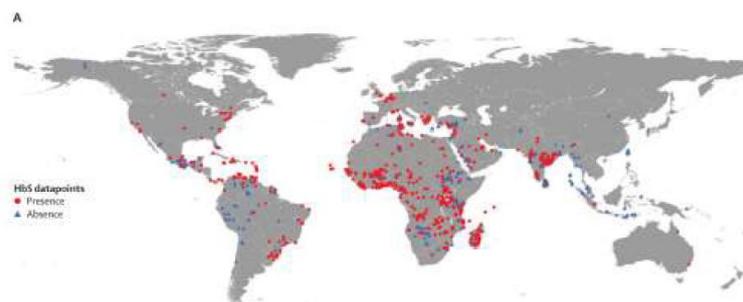
Global distribution of malaria before introduction of comprehensive protection measures

If a child inherits gene mutation from both parents, it is going to suffer from sickle cell disease. Those who have only one mutated gene are better protected

In Africa, India and the Middle East gene distribution of sickle cell and malaria risk are overlapping.

The global distribution of sickle cell genes in the world is in Africa, around the Mediterranean Sea, in India and spotted in other areas. Around 5 % of the carriers of the S gene have 2 S genes and are sickle cell patients.

Global distribution of Sickle cell gene S (carriers AS and disease SS) (Lit. 2)



2 Fetal Hemoglobin

Fetal hemoglobin, (also hemoglobin F, HbF,) is the main oxygen carrier protein in humans before birth. Hemoglobin F is found in fetal red blood cells, and is involved in transporting oxygen from the mother's bloodstream to organs and tissues in the fetus. It is produced at around 6 weeks of pregnancy and the levels remain high after birth until the baby is roughly 2–4 months old. Hemoglobin F has a different composition from the adult forms of hemoglobin, which allows it to attach to oxygen more strongly. This way, the developing fetus is able to retrieve oxygen from the mother's bloodstream, which occurs through the placenta found in the mother's womb.

In sickle cell disease, it was found that increasing the production of hemoglobin F is a way to relieve some of the symptoms.

Cure of sickle cell disease is possible only with stemcell transplant

(this treatment is dangerous, not available in our partner countries and performed rarely even in industrialised countries)

without treatment many children die at an age of 5 to 8 years

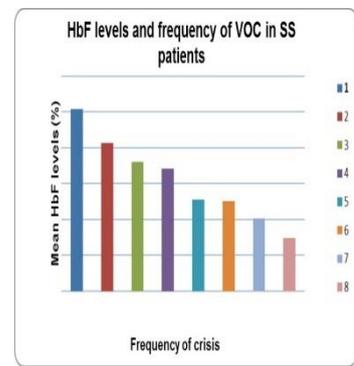
But: after increase of hemoglobin F to 30% symptoms decrease or even disappear

fetal hemoglobin

- is the transport protein of iron during pregnancy
- production is stopped after birth
- cannot be detected any more after 4 months

2.1 Allopathic treatment: Hydroxyurea to increase Hemoglobin F

In a study in the New England Journal of Medicine, it was found treatment of patients with hydroxycarbamide (hydroxyurea), an antineoplastic (tumor-inhibiting) drug, increased the quantity of fetal hemoglobin in erythrocytes. It also appeared to break down cells that were likely to sickle, further decreasing the risk of vaso-occlusive sickle-cell crises.



But hydroxyurea, which is an old chemotherapeutic agent, has many side effects and can lead to cancer.

Additionally folic acid is given and in children antibiotic prophylaxis treatment with Penicillin is given to children until the age of 5.

Recently the FDA (Food and Drug Agency) in the US approved two new drugs: Adakveo, made by Novartis, can prevent episodes of nearly unbearable pain that occur when malformed blood cells get stuck in blood vessels. It is approved only for patients aged 16 and over, it is delivered as an infusion once a month.

Fetal Hemoglobin can be induced:

- *In allopathic medicine*

Hydroxyurea is the standard treatment of sickle cell disease

Hydroxyurea is an old chemotherapeutic agent, it has severe side effects and may cause cancer

Adakveo (Novartis), reducing crisis attack

Oxbryta (global blood therapeutics), reducing anaemia registered by FDA in 2019

cost of treatment: 100 000 \$ per year

Oxbryta, made by Global Blood Therapeutics, can prevent severe anemia from the disease that can lead to permanent damage to the brain and other organs. Taken as one tablet daily, the drug is approved for patients aged 12 and older.

The costs for these drugs are 100.000 \$ a year, they must be taken lifelong and are only available at an age when the damage of the organs has already occurred. Many patients in Africa or India have then already died.

3 Experience with plants to increase Hemoglobin F

There is experience with beneficial effect of plants in sickle cell disease. It was found that this effect is caused by the induction of hemoglobin F. In Nigeria and Burkina Faso herbal medicines are prepared and sold in the market.

- **In Phytotherapy**

Many plants are able to induce Hemoglobin F

- **Nigeria:** according to the experiences of Yoruba tribe the medicine **Niprisan** was developed out of 4 plants, after clinical studies registered in the US (available by the Government in Nigeria)

Ciklavit was developed and studied out of pigeon pea *Cajanus cajan* (available)

- in Burkina Faso **FACA** is prepared out of 2 plants



1. Nicosan (Niprisan)

Niprisan was developed in Nigeria out of 4 plants: Piper guiniense, Clove, Pterocarpus and Sorghum bicolor.

Scientific studies showed a reduction in symptoms of sickle cell disease. It was evaluated in cooperation with a pediatric hospital in the US and received the registration of the Food and Drug Agency FDA.

Medicine from Nigeria : Niprisan and Ciklavit

Niprisan a combination of 4 plants from Yoruba folk medicine

United States Patent (19) (11) Patent Number: 5,800,819
 Wambebe et al. (45) Date of Patent: Sep. 1, 1998

(54) PIPER GUINEENSE, PTEROCARPUS ORU, EUGENIA CAPSICIFOLIA, AND SORGHUM BICOLOR EXTRACTS FOR TREATING SICKLE CELL DISEASE (56) References Cited U.S. PATENT DOCUMENTS 4,473,538 9/1981 Baboin 424951



In the scientific study all patients had Niprisan and placebo, one group started with Niprisan, one with placebo. Then it was counted how often patients had a painful sickle cell crisis. It was found that the incidence of having a crisis was much less during the time when they had Niprisan. (Significance in a scientific study means that the difference is true not just by chance.)

Niprisan study (Lit 3)

Blinded randomised cross over study

Group A: 6 months of 12,5 g of Niprisan, one month of wash out, 6 months of placebo

Group B: 6 months of placebo, one month of wash out, six months of 12,5 g of Niprisan (wash out = no medicine)

**Results: 0,05 crisis per month with Niprisan
 0,11 crisis per month with placebo**

significant difference p = 0,05

The licence to produce the medicine was given to a pharmaceutical company, but there was corruption and mismanagement. Prices increased and the medicine was not affordable anymore.

Since 2015 the medicine is distributed by the Nigerian Government for 300 Naira, (less than 1 Euro). There is no information whether the medicine is available outside Nigeria. There is no information about the recipe.

2. Ciklavit made of *Cajanus cajan*

This herbal medicine was made in Nigeria, there is no information how to prepare it. It is made out of an extract of *Cajanus cajan*, pigeon pea, zinc and vitamin C is added. The placebo is made only of zinc and vitamin C.

Scientific study from Lagos, Nigeria ^(Lit.4) aqueous extract of *Cajanus cajan* (pidgeon pea) = Ciklavit is compared to Placebo (no treatment)

Ciklavit = extract of *Cajanus cajan* + Zinc + Vit.C

Placebo = Zink und Vit. C

results:

Phenylalanin
(= amino acid in the plant)
is responsible for 70% of
the activity



i

There is one scientific study to evaluate the effect of Ciklavit in 100 patients. 45 patients could be analysed in the treatment group, 42 in the control group.

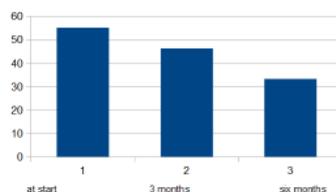
The size of the liver is a sign of liver function. If the liver is too big, which is called hepatomegaly, the liver function is impaired. There was a trend to improvement, liver size going back to normal, in the patients

who received Ciklavit, and a trend to increase of liver size as sign of worsening in the control patients, but the difference was not significant. Liver function test also improved in another study.

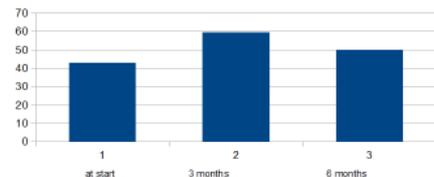
Ciklavit study results I:

Hepatomegaly, trend of improvement in Ciklavit group, but not significant (p = 0,1)

% of hepatomegaly in sickle cell patients, Ciklavit group



% of hepatomegaly in sickle cell patients, control group



Increase in control group not significant (p= 0,2)

Looking at the incidence of painful crisis, patients had significantly less pain attacks if they took the Ciklavit medicine. Ciklavit as a medicine is available only in Nigeria (to my knowledge)

But the plant is available in many countries in Africa and in India. Using *Cajanus cajan* to prepare daily meals could be helpful.

Ciklavit Study results II:

looking at painful crisis as symptom of vessel block

Comparison between the periods of 6 months without Ciklavit and 6 months with Ciklavit

less events of crisis during time of Ciklavit intake

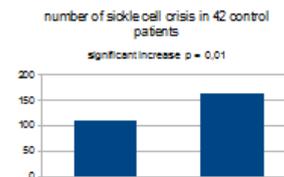
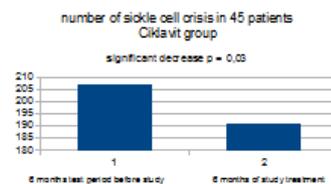
$p = 0,03$

significant difference

more events of crisis during time of control

$p = 0,01$

(in scientific studies a statistical value of p is calculated to be sure that the difference found is real and not just by chance)



There is some experience from participants of Anamed seminars in Africa.

Practical experience from Benin

Marcelin Aigbé

- Take daily one meal with *Cajanus cajan* pigeon pea
- Take daily decoction of *Cajanus cajan* fresh leaves, boil for 20 minutes, drink in course of the day
Dose: children up to 6 years 50 g in 200 ml of water,
6 to 12 years 100 g in 400 ml of water,
adults 250 g in 1 l of water
- Add fagara root to this decoction in case of crisis (see slide 11)

after 3 months, stop treatment for 2 weeks and evaluate the patient.

My comment: as sickle cell disease is not curable, frequent meals with *Cajanus cajan* (like in the experience from Senegal) and decoction with *Cajanus cajan* leaves should be continued.

Experience from Senegal (Brother Nicolas)

- Twice a week a meal with *Cajanus cajan*
- additionally:
 1. week: take a handful of fresh leaves of *Cajanus cajan*, boil it for 5 Min. in 1l of water, drink it in 3 portions during a day
 2. week: prepare and drink decoction in the same way with leaves of *Zanthoxylum fagara*

After 4 weeks of treatment control the symptoms, if the patient is well, decoction can be stopped for one month and then be repeated. Meals with *Cajanus cajan* need to be repeated twice a week

It is worth trying.

When I visited a place in Gujarat in India, (see the information later about Sr. Lissy and the treatment with Aloe vera and jaggery) I learned that the normal food in this area is rice and dal, and in this area dal is prepared mostly of pigeon pea. Still sickle cell patients had strong bone pain as a symptom of sickle cell disease. But I do not know whether all these patients took *Cajanus cajan* as their regular food.

3. *Zanthoxylum fagara*

There are many publications about the use of *Zanthoxylum fagara*. It is included in the FACA medicine from Burkina Faso, added to the Cajanus cajan treatment in Benin and Senegal. There is another proposal from Uganda. It is difficult to prepare this medicine, but it can be stored and given to patients, doses are available. There is no clinical study to my knowledge.

Zanthoxylum fagara root bark

Dr. Patricko Engeu, Uganda

- Soak 100g of **Fagara root bark** in 300 ml of vinegar for 24 hours, filter and press so that you get 200 ml
- Boil 500 g of **lemongrass** (*Cymbopogon citratus*) in 1 l of water, filter to get 900 ml
→ add both: 200 ml + 900 ml = 1100 ml

Dose:

up to 5 years 1 x 5 ml daily
6 - 12 years 1 x 10 ml daily
13+ years 1 x 15 ml daily
Expiry date after 1 year



4. FACA

FACA was developed in Burkina Faso
Videos:

<https://www.youtube.com/watch?v=ru3B4QNGee4>, in French on youtube
https://www.youtube.com/watch?v=EFIP_eScISQ, with English translation about the disease and life with the disease
https://www.youtube.com/watch?v=vVYyjAl_LmM

Two plants with known activity against sickle cell disease are the ingredients of this herbal medicine: *Zanthoxylum fagara* and *Calotropis procera*.

Faca (Lit.5)

Zanthoxylum fagara + *Calotropis procera*

sodom apple, rubberbush

In Burkina Faso a herbal medicine was developed out of the powder of these two plants (*available only in Burkina*)

results:

- clinical study with only few participants
- scientific proof not yet sufficient
- treatments shows good results



(picture: *Calotropis procera*)

There is one study evaluating the effect of Faca comparing four treatment groups: *Zanthoxylum*, *Calotropis*, the combination of both and Hydergine, a mixture of salts of three dihydrogenated ergot alkaloids. (*There are data about a widening of blood vessels by Hydergine, this may be the reason why this medicine was evaluated in the study.*) There is no randomisation, (which is the gold standard of scientific research) the number is very small. No more studies are published. The study is critically discussed in the scientific community. The medicine is available only in Burkina Faso.

5. *Carica papaya*

The first publication about a herbal treatment of the Yoruba tribe in Nigeria was in 1987, 19 years later another publication looked at it in a lab experiment.

They used what they called unripe fermented papaya. The antisickling effect was not seen with ripe papaya.

Fermented raw *Carica papaya*: (Lit.6)

cut 100 g raw (unripe) peeled papaya, mash into small pieces (0,5 cm), put it into 100 ml of water, keep at room temperature during 48 - 72 h, drink without filtering

Dose:

2 - 6 years: 3x5 ml daily
7 - 11 years: 3x10 ml daily
12 + years: 3x15 ml daily



proceeding: calculate daily dose, prepare every second day for 2 days (take one dose after 2 days, one dose after 3 days), no fridge necessary

good results, no side effects in studies

African Journal of Biotechnology Vol, 5 (20), pp. 1947-1949, 16 October 2006 Further evaluation after 19 years
Available online at <http://www.academicjournals.org/AJB>
ISSN 1684-5315 © 2006 Academic Journals

Antisickling agent in an extract of unripe papawpaw (*Carica papaya*): Is it real?

T. ODUOLA¹*, F. A. A. ADENIYI², E. O. OGUNYEM³, I. S. BELLO⁴ and T. O. IDOWU⁵

Lab study

Antisickling and reversal effect best at concentration of 1 g unripe papaya pulp in 1 ml of saline, kept at room temperature for 48 hours.

It is real!

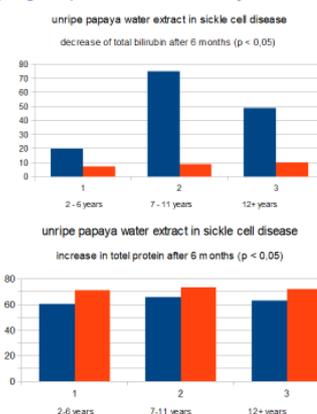
Raw fermented papaya is safe

In another study the raw papaya was kept with water for 72 hours at room temperature, the same effect was seen.

In the study the investigators looked at bilirubin which is high in sickle cell disease as the red blood cells are destroyed after 20 days instead of 120 days in normal red blood cells. In all age groups the bilirubin decreased after intake of the medicine. (blue bars = before intake of the medicine, red bars = after intake for 6 months).

Fermented raw papaya

results: improvement of liver function after intake for 6 months, age groups 2-6, 7-11, 12+ years



decrease of bilirubin
less hemolysis (destruction of red blood cells)

p<0,05 (significant)

increase of total protein
(indirect sign of improved liver metabolism)

p<0,05 (significant)

Protein is built in the liver. Increased protein after intake of fermented papaya is an indirect sign of improved liver function.

Practical problems

The medicine needs to be prepared at home. As the result is the same whether fermented papaya is kept for 48 or 72 hours, it is possible to prepare the dose of 2 days and take half of it after 48 hours, half after 72 hours. In some cases raw papaya is not always available. In this situation another treatment option must be chosen. The responsibility to prepare the medicine is given to the mother.

How to know how much to prepare

Prepare the medicine first in the dispensary where a weighing machine is available and the volume can be measured. Take 100 g of raw papaya, 100 ml of boiled water, cooled down, and a pinch of salt. Keep for 48 hours, then check how many ml you have. Then give the medicine to the patient according to the age adjusted dose: 2-6 y: 3 x 5 ml, 7 – 11 y: 3 x 10 ml, 12+ y 3 x 15 ml per day

How to measure 5 ml? Teaspoons may have different sizes. There are often coughing syrup bottles with a measuring cup giving information about 5 and 10 ml. If it is not available in the family, try in the dispensary and measure it. Or you take what is available and increase the dose if there is no effect. If this medicine does not work, you may not have given enough.

6. *Ocimum basilicum*

This plant has been studied in Kinshasa.

There are only lab tests, normally these tests are following the experience of people who use the plant for a special disease.

In the study the results for a methanol extract and an extract with water were the same.

They found that sickled cells of patients in the lab normalised if the extracts with *Ocimum basilicum* were added. Cells were in the normal round shape after adding the extract.

Ocimum basilicum

research from Kinshasa, Kongo (Lit.7)

Publication of laboratory work, no clinical data

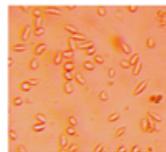


How to prepare: pour 1l of boiling water on 300g of dried *Ocimum basilicum* leaves. In practical maybe 50 ml can be poured on 15 g of dried leaves. If you do not have dried leaves, you can take 4 times more from the fresh leaves (see note for ratio below at moringa). As there will not be a weighing machine in the family you need to prepare the medicine first in the center and then give the measurement to the family.

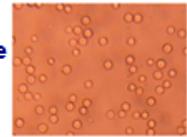
Mode of preparation in the lab: pour 1 l of boiling water on 300 g of dried leaves

Prof. Pius Mpiana, Kinshasa

results: **sickled red blood cell normalise**



without treatment



after treatment with extract of *Ocimum basilicum*

red blood cells in sickle cell patients

Anthocyanins are important for the effectivity, they are destroyed by heat, therefore basilicum leaves should not be boiled, just pour boiling water.

Dose: no information available

Proposal: pour 50 ml of boiling water on 15g of dried basilicum leaves,

3 x 15 ml daily?

Should be prepared every day, dose can be increased, is well tolerated

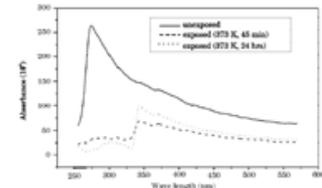


Fig 4. UV-visible spectra of anthocyanin fraction unexposed and exposed to heat at 373 K during 45 min and 24 h.

There is no dose given, (I contacted the head of the institution who published it, no information). But *Ocimum basilicum* is available and not toxic. If nothing else is available, just try and increase the dose.

A feedback is most welcome.

7. Fermented *Moringa oleifera*

For fermented Moringa there again is only information from work in the lab. If you put red blood cells of a sickle cell patient into a petri dish all cells will form sickles after some time. After adding the fermented moringa 80% of the cells were prevented from sickling after 2 hours of exposure. (blue bar). Adding the extract to cells which had been made sickle cells (by a special chemical) the cells went back to normal (red bar). Unfortunately there is no information about a dose.



petri dish

Fermented *Moringa oleifera* (Lit.8)

procedure: put 500 g of dried Moringa leaves in 2 l of water, keep 3 days at room temperature, then filter

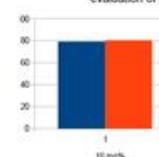


Experimental results in the lab:

- after adding fermented Moringa to patient's blood:
 - after 2 hours: no sickling of cells for 80% of the red blood cells (blue bar)
- adding fermented Moringa to blood of patients with already sickled cells:
 - after 2 hours: change of sickled red blood cells into normal shape

antsickling (blue) and reversal effect of moringa leaf powder aqueous extract

evaluation of sickle cells in vitro after 120 min



same result for 10% and 20% solution

Practical problems Fermented Moringa needs to be prepared for every day. Example: Put 12,5 g of dried Moringa leaves into 100 ml of water, keep for three days then take in three portions throughout the day. If you do not have dried leaves, you can take 4 times more fresh leaves (50 g). This corresponds to a ratio calculated by Mark Reese (<https://www.ahealthyleaf.com/info-and-news/how-many-lbs-of-fresh-moringa-leaves-does-it-take-to-produce-1-lb-of-powder/>)

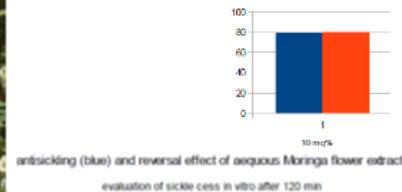
As there will not be a weighing machine in the family you need to prepare the medicine first in the center and then give the measurement to the family.

Moringa flowers: It is possible to have the same effect in the lab with Moringa flowers kept in water for three days. In the study the same amount of dried flowers (300g) were mixed with 2 l of water for 3 days. Prevention of sickling and reversal of sickling were seen at 80%.

Another study looked at the antisickling activity of Moringa leaves. In this lab study, antisickling activity was shown, but a fridge is needed, so it is not possible to use in a village.

Same effect with water extract of *Moringa oleifera* flowers

10% solution prevents sickling of patient's blood in the lab (blue) and normalizes sickled red blood cells (red)



In another experiment 50 g of dried Moringa leaves were mixed with 150 ml of water, kept in a fridge for 15 h, filtered and kept in the fridge until use (Lit.9). (as there is no fridge in the village, we do not know how to transport the approach to the village level)

experience from patients in the US (Blog): Improvement after 2 teaspoons of Moringa powder daily (but we do not know what other medicines they took)

just try if there is no other treatment!!

Experience from patients who inform in blogs in the US

In blogs in the US many sickle cell patients report an improvement of their general status when they take Moringa powder regularly. There is no study about it. It may be an option to give this advice to families with sickle cell patients if there is no other medicine.

8. Ayurvedic recipe *Aegle marmelos* and *Piper longum*

This ayurvedic recipe is based on experience, there is no scientific data.

Treatment proposal with bael fruit and long pepper :

dry the fruits of both plants and make it into powder

dose: 500 mg = 4 – 5 knife points of bael fruit powder
1 knife point of long pepper powder

take twice a day before meals 2 months treatment
1 month break

lifelong

Ayurvedic recipe

***Aegle marmelos* (bael fruit) + *Piper longum* (long pepper)**
Both available only in South East Asia

bael fruit



long pepper



This medicine can be prepared in advance in the dispensary and then sold to the families of patients.

Why does it work? There is a molecule in the fruit of *Agle marmelos*, Angelicin. The effect of this molecule was analysed in a lab in Ferrara.

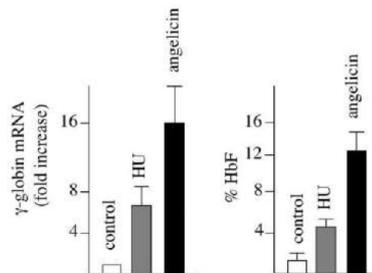
It was seen that the molecule Angelicin increased the concentration of fetal hemoglobin and the substance in the cell which leads to the production of hemoglobin F. (messenger RNA). Its activity was even stronger than the effect of Hydroxyurea (HU).

Accumulation of γ -globin mRNA in human erythroid cells treated with angelicin

Lampronti I, Bianchi N, Borgatti M, Fibach E, Prus E and Gambari R. Accumulation of γ -globin mRNA in human erythroid cells treated with angelicin. Eur J Haematol 2003; 71: 189-195. © Blackwell Munksgaard 2003.

Publication about in vitro activity of angelicin present in Bael tree, Ferrara Italy

mRNA and fetal hemoglobin increase after incubation with angelicin, more than with HU



9. *Curcuma longa* (Turmeric in India)

A methanol extract of *Curcuma longa* rhizome prevented sickling of red blood cells in the lab. There are no clinical data, neither of the methanol extract nor of the plain rhizome.

As Turmeric is used as spice for food, it may be a good advice to use it for preparation of the daily food.

Curcuma longa (Lit.10)

In a publication from Kinshasa/Kongo the investigators found antisickling activities of a methanol extract of *Curcuma longa*, the most effective part was the rhizome.



sickled blood without plant



normal blood cells after adding *Curcuma longa* extract

No clinical data.

Maybe wise to include *Curcuma longa* into daily diet

10. *Aloe vera* (*Aloe barbadensis*)

There are only 2 publications about the antisickling effect of *Aloe vera*.

Aloe vera gel was prepared and its antisickling activity was compared to not treated red blood cells as control, to Vitamin C and Phenylalanin, an amino acid which is known for having an antisickling activity.

Aloe vera barbadensis

lab experiment: prevents sickling of red blood cells in sickle cell patients (Lit. 11), Nigeria



After 30 minutes all control red blood cells had sickled, there was no inhibition of sickling. About 90% of cells exposed to vitamin C, 95% of cells exposed to Phenylalanin and 98% of those who had been exposed to *Aloe vera* Gel were inhibited from sickling and remained normal. The full *Aloe vera* leaf was also used in this comparison but it is difficult to prepare and cannot be used in a village.

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The effect of aloe vera plant (*aloe barbadensis*) extracts on sickle cell blood (hbss)

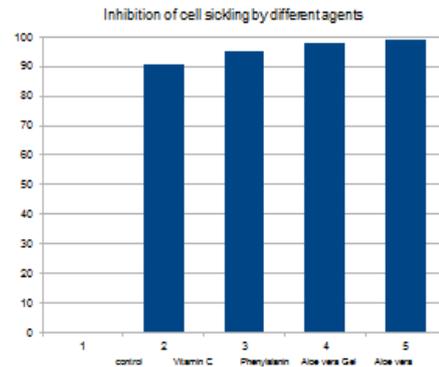
Nwaoguikpe R. N¹, Braide, W² and Ezejiolor³, T.I.N

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In the experiment 200 ml of liquid *Aloe vera* gel in comparison with control, Vitamin C and phenylalanin (amino acid) were prepared, to prevent sickling of blood of sickle cell patients

Results:

- no inhibition in control
- 90,74% inhibition with Vitamin C
- 95,34% inhibition with Phenylalanin
- 98,09% inhibition with *Aloe vera* gel
- 99,23% inhibition with *Aloe vera* leaf



There is clinical experience in Gujarat, India.

Sr. Lissy Paul CCV is practicing herbal medicine since more than 14 years.

She got the information about the treatment of sickle cell disease from a (late) priest in Andra Pradesh.

The treatment is very successful, if patients or a member of the family come to take the tonic once a month, the symptoms are not seen any more after one week.

How to prepare: Cut the *Aloe vera* leaf lengthwise, scratch the gel and collect 1 l. Boil it, filter. Then add 500 g jaggery (non centrifuged cane sugar), boil again and filter. Let it cool down. Put the tonic into 500 ml bottles. Keep it in a fridge in the health center. Inform patients at home to keep it in a plastic bag put into a mud pot with water.

Aloe vera and brown sugar(jaggery) for the treatment of sickle cell disease

Experience of Sr. Lissy Paul CCV, Gujarat/India (Anamed Teacher)

How to prepare: boil 1 l of *Aloe vera* gel, filter, add 500g brown sugar (jaggery), boil and filter. Keep in a bottle

Dose: up to 12 years 2 x 10 ml daily
 12 – 18 years 2 x 20 ml daily
 adults 2 x 30 ml daily

patients come to the health center once a month and buy a 500 ml bottle, depending on the dose there is a break

In the health center bottles are kept in a fridge, at home patients put the bottle in a plastik bag and keep it in a mud pot with water.

result: no more symptoms after 1 week of treatment

260 patients are treated during the last 2 years

Data are collected to prepare a scientific publication.



Patients or family members come once a month to get the medicine. Patients take it according to their age in different doses. Then there is a break of treatment when the bottle is finished, duration of taking the medicine depends on the dose. They start again after one month.

I met this boy in October 2019. He looked miserable, had stopped going to school and had to go to a hospital every second or third month. The allopathic treatment hydroxy-urea was not given according to state of the art. Summarising the cost of treatment in these 13 years, the family spend more than 80.000 Rupies (1000 €), still the boy had a miserable life.

After 4 months with Aloe vera and jaggery you can hardly see that this is the same boy.

Example from Gujarat: no more symptoms after 4 months of treatment with *Aloe vera* and jaggery (Ayush, 16 years)

diagnosed at the age of 3 ½ years

• Symptoms

weakness
bone pain
anaemia
stopped going to school

• Allopathic treatment

pain killer (Ibuprofen)
folic acid
some blood transfusions
occasionally malaria treatment



october 2019



january 2020

treatment costs: 1000 € in a „specialty clinic for sickle cell disease“ in Gujarat, the normal allopathic treatment of hydroxyurea was not given

11. Wheat grass *Triticum aestivum*

Wheat grass is not a treatment for sickle cell disease. But there are lab tests suggesting that it can be effective to treat a complication of sickle cell treatment.

Iron overload

There may be too much iron in the body of sickle cell patients. One reason is that the red blood cells have a shorter life span than normal cells. When the red blood cells are destroyed, the iron of these cells remains in the body. The other reason is that sickle cell patients need many blood transfusions because of their anemia, which is another source of iron.

Problem of iron overload

Iron can be excreted by the kidney only when it is bound to another molecule (building a chelat complex)

If iron remains in the body, it damages the cells where it is stored, mainly in liver, heart, pancreas (Gutbread) and becomes a thread for these organs and life

Patients with sickle cell disease can have an iron overload because of

- haemolysis (= destruction of red blood cells)
- blood transfusions, given to treat anaemia

Our body is not able to excrete this iron through the kidneys. Iron needs to form a complex with another molecule. If there is too much iron in the body it is embedded in other organs like liver, heart, brain, kidney, which can lead to a life threatening situation. This is called **iron overload**. In allopathy a medicine called Desferoxamin is given after more than 20 transfusions, if one lab value, **ferritin**, exceeds 1000 mg.



Wheatgrass *Triticum aestivum*

binds to the iron molecule and enables the iron to be excreted in the urine

An animal experiment showed that wheatgrass increased the urine excretion and decreased the iron concentration in the blood in experimental iron overload (Lit.12), but there is no publication about the use in sickle cell disease.

how to prepare: - sow the wheat, harvest at a height of 20 cm
- prepare 100 ml of juice in a mixy or handgrinder
- prepare and drink daily
when to use: after 10 - 20 blood transfusions

no side effects!

Wheat grass was half as effective in the animal experiment compared to the allopathic treatment with desferoxamin with many side effects

Wheat grass has been shown to increase the urine output of iron in a study with mice, it was also shown that the iron concentration in the blood serum decreased. This mechanism could reduce the danger of too much iron in the body after multiple blood transfusions. Clinical data are not available.

Information from the animal study:

In the first 2 columns, normal **urine output** of iron is seen in NC column, increasing only little if the animals are getting too much iron (DC column)

Urine output of iron is very high in the animals getting allopathic medicine Desferoxamin (DCD column).

Total phenolics are the molecules that enable chelation

In metanolic extract 506,92 , in aqueous extract 198,5 µg/ml

Mouse experiment: increase in urin iron secretion

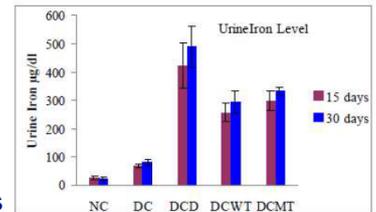
NC – controls

DC – experimental iron overload

DCD desferroxiamine (allopathic standard)

DCWT waterextract wheatgrass

DCMT methanolic extract wheatgrass



After having water extract of wheat grass the urine output of iron is almost three times higher than without treatment, but half of the effect of allopathic medicine. There are no side effects of the herbal treatment. The effect of the methanol extract is only slightly better compared to water extract.

If we look at the **iron concentrations in blood serum** (serum is blood without cells), we see the normal low concentration in NC column, the maximally high concentration in experimental iron overload (DC). After allopathic medicine the concentration is lower (DCD column) than the maximum, but still very high compared to normal.

Mouse experiment: Serum iron level

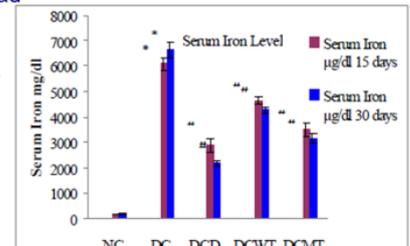
NC: controls

DC: experimental iron overload

DCD: desferoxamine (allopathic standard)

DCWT: waterextract wheatgrass

DCMT: methanolic extract wheatgrass



Result: activity of water extract of wheatgrass around half of allopathic standard

Wheat grass water extract is less effective than allopathy; the methanol extract is more effective than water extract, but also less than allopathic desferoxamine treatment.

How to prepare: see attachment how to grow wheatgrass

Conclusion

Wheat grass juice may be an attempt to reduce the danger of too much iron in the body after many blood transfusions. It is worth trying after more than 10 transfusions. **BUT:** there are unfortunately no data available.

4 What else is needed?

4.1 Antibiotics

The spleen is often the first organ which loses function, as the vessels of the spleen are obstructed by sickle cells. The spleen is a very important organ where cells, important for the immunity of our body are produced. That is the reason why patients with sickle cell disease are threatened by infections (an example: one teenage girl with sickle cell disease, whose symptoms were well controlled with Aloe vera and jaggery tonic went home for holidays. She got diarrhea, parents did not send her to the hospital, and she died due to the diarrhea).

What else is needed?

- Antibiotics (standard in the US: penicillin until the age of 5)
most plants used in sickle cell disease have an antibiotic activity
like Aloe vera, moringa, papaya, basil (Tulasi)

**If these plants are used,
prophylactic antibiotics are not necessary!**

- Folic acid Folic acid tablets are often distributed to sickle cell patients, should be taken regularly, (available in food: spinach, dal, peas, peanuts, beans, papaya)
- Drink enough to prevent thickening of the blood, take care of clean drinking water
- Malaria prophylaxis: for sickle cell patients (SS) Malaria is life threatening (Lit. 13)

In the US, children receive penicillin until they are 5 years. All plants which can be used to treat the symptoms of sickle cell disease have an antibiotic activity and can help to fight infections. If an infection occurs the patients should be treated, either with antibiotic plants or allopathic antibiotics.

4.2 Folic acid

Folic acid is a vitamin which is needed for the production of red blood cells. As in sickle cell disease red blood cells are stable only 20 days instead of 120 days, much folic acid is needed. In many situations folic acid tablets are distributed by the local government or health services. In these cases it is important to take these vitamins. If it is not given, patients should take food rich in folic acid.

Folic acid daily

Younger than 6 months: 0.1 mg/day, ages 6 months to 1 year: 0.25 mg/day

Age 1-2 years: 0.5 mg/day Older than 2 years: 1 mg/day

Cochrane review: only 1 study, not convincing

Vegetables and fruits high in folic acid

- Spinach 1 cup = 0.263 mg
- Lentils 1 cup = 0,359 mg
- Green peas 1 cup = 0,101 mg
- Peanuts 1 cup = 0,088 mg
- Beets boiled 1 cup = 0,136 mg
- Papaya 1 piece 0, 115 mg



Adults need 1 mg of folic acid daily, children less.

4.3 Drinking enough water

It is very important that sickle cell patients drink enough water. To prevent infections this water needs to be clean, better boiled. If the body does not have enough water, the blood thickens and the danger of sickling of red blood cells increases. The table lists the need of drinking water or other fluid for a population outside of tropical countries. The amount needed in tropical countries is higher.

Importance of drinking enough is severely underestimated

If there is enough fluid in the blood vessels, the danger of sickling is reduced.

the amount of fluid needs to be higher for a population in tropical countries

		Total water adequate intake (Foods and fluids)	
Infants	0-6 months	680 mL/d (THROUGH MILK)	
	6-12 months	800-1000 mL/d	
	1-2 years	1100-1200 mL/d	
Children	2-3 years	1300 mL/d	
	4-8 years	1600 mL/d	
	9-13 years	Boys	2100 mL/d
		Girls	1900 mL/d
> 14 years	cf adults		
Adults	Men	2500 mL/d	
	Women	2000 mL/d	
Pregnant women		+ 300 mL/d vs adults	
Lactating women		+ 600-700 mL/d vs adults	
Elderly		Same as adults	

4.4 Malaria prophylaxis

For sickle cell patients malaria infection is very dangerous. The scientific literature recommends giving malaria prophylaxis to sickle cell children (Lit.13). A study from Uganda evaluated whether the number of malaria attacks could be reduced if Artemisia annua tea (5g in 250 ml) was taken once a week. It was shown that in comparison with a control group without prophylaxis in 132 workers of a flower farm a significant number of artemisia tea taking patients had just one or no malaria infection.

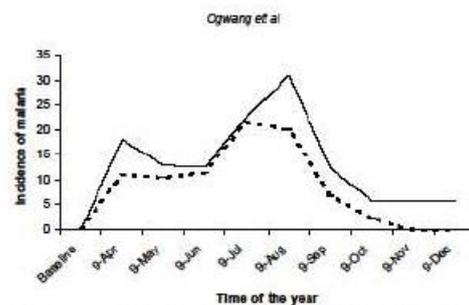


Figure 2: Monthly incidence of malaria in Artemisia (dashed line) and placebo (unbroken line) groups

In a recent intervention in India 400 inhabitants of a malaria endemic area received 5 g Artemisia annua tea per day for one week and thereafter once a month. No malaria infections were observed (Sr.Britto HC, Hazaribagh, India, not yet published).

Conclusion

Herbal medicine in sickle cell disease

- Locally available or easy to buy
- Easy to prepare, even at home
- Reduces or even stops symptoms
- No side effects reported

prevents early death

*in case of questions please send a mail. Text is available in
German, English, French and Portuguese*

Literatur

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