Abrus precatorius (Fabaceae)

(Synonym Rhynchosia precatoria)

English: Jequirity bean, rosary pea, prayer bean, precatory bean, Indian liquorice French: Pois rouge Spanish: Tento muido Arabic: Ain-ed-dik Chinese: Siang-sz-

tsze (root of S.) India: Gunj, Gungachi, Guri-ginja Tamil: Kundumani

German: Paternostererbse

Name of the seeds: Prayer beads, Crab's eye

Pharmaceutical definition: Jequiriti semen, Abri semen

Description of the plant

A climbing vine indigenous in India and Indonesia, leaves alternately compound, flowers arranged in clusters, violet or pink. The seed pod curls back when it opens and reveals the seeds. The seeds are flat and truncate shaped, 1.5. – 2cm long, with attractive scarlet colour. **They are highly poisonous.**

Plant parts used

The dried red-black colored seeds, often in ground state as component of wholesomness powders; more rarely the leaves and roots.

Constituents:

Abrus precatorius beans are known to be under the most toxic plant parts worldwide (1). There are reports of fatal outcomes of men, who ate one or two beans only. Swallowing of intact beans is nearly harmless. Boiled seeds eaten by the residents of the Andaman Islands were harmless, too. They were analyzed for proteins, amino acid composition, minerals and antinutrional factors with positive results (27). In the **seeds** the toxic principle is abrin, a mixture of at least five lectins, abrin A - D, and abrus-agglutinin. The abrins consist of two peptide chains connected by a disulfide bridge. Abrin A consists of an A-chain with N-glycosidase activity, which inhibits protein synthesis, and lectin-like B-chain responsible for binding with cell-surface receptors and penetrating of abrin-A molecule into the cell (24). After purification they can be separated by affinity chromatography followed by gel filtration on a DEAE –Sephacel column. The relative molecular weights of abrin A – C are around 64.000, that of two agglutinins 128.000 (7,16). For further identification the crystal structure was investigated (37). The abrin A crystals belong to the monoclinic space group P 2 (36). The sequence of amino acids of the B-chain in both abrin-A and abrin-B were elucidated by enzymatic digestion with trypsin. They consist of 268 amino acids and share 256 identical residues (12). To elucidate the mechanism of intoxication the active glycotopes for the attachment were determined. This chemical structure is assumed to be responsible for the toxic effects (41). Abrins disarrange the proteinbiosynthesis by interfering with the 60 S-ribosomes of animal cells, irreversibly. The toxicity of these abrins is variable, but they are the most potent toxins of the world, comparable with the botulinus toxin. The fifth of them, abrus agglutinin, is not so very toxic against cells, but it exhibits agglutination toward animal erythrocytes (8).

From the chloroform soluble fraction of the concentrated 80 % methanol extract of A.precatorius **seeds** a new flavonol glycoside was found with following dates: C_{29} H_{34} O_{16} , M+638, mp 260-262 0 C (42).

In **leaves** and **roots** sweet saponins are found, comparable with liquorice ("Indian liquorice").

From the acid hydrolyzed methanol-soluble extract of **leaves** of A.precatorius four triterpenoids named abrusosides A-D were isolated, of which one was known, another one was unknown. These compounds were neither acutely toxic in mice nor mutagenic in Salmonella typhi murium. According to a human taste panel the sweetness was 30-100 times greater than sucrose (3). Their structure was elucidated by spectroscopic techniques including 2D-NMR (10).

Two triterpenoids saponines 1 and 2 were isolated from the **aerial parts** of A.precatorius and ethylacetate derivatives were prepared. Tested for inflammatory activity in the croton oil ear modell all showed inhibitory activity, the ethylacetate derivatives in a greater extent (1).

From the **aerial parts** of A.precatorius two isoflavanchinones were extracted with dichloromethane. After column chromatography on Sephadex LH 20 with methanol they were identified and named. One of them was the known abruquinone B and the new one abruquinone G. Chemical structures were identified by spectral analyses (15). All abruquinones show biological activities (16).

From the **roots** of A.precatorius five isoflavanquinones were extracted by methanol and separated by partition chromatography on a silica gel column. Three of them were new and were designated as abruquinones D, E, and F (13).

Traditional uses

In the Ayurvedic medicine leaves of Abrus precatorius are laxative, expectorant and aphrodisiac medicines. Seeds are said to be purgative, emetic, tonic, antiphlogistic, aphrodisiac and antiopthalmic. For the indigenous people they are potent phytomedicines, many of them in mixtures with other plants. Their toxicity is underestimated.

They are even sold via internet (Tan-Hord Exports List of herbs). In some countries of Asia beans are used as weights and jewellery is made from them by drilling. In Tanzania traditional healers claim the competence in the treatment of epilepsy. A. precatorius can be found between 60 plants commonly used against this illness (18). In Zimbabwe extracts of 58 plants popularly known to be effective against schistosomiasis were tested in vitro against excysted cysticercoids. Extracts of stem and root of A.precatorius were under the ten most effective samples (17,20). In the Indian Central Drug Research Institute in Lucknow discussions about an antifertility program are going on. One of the plants with priority is A.precatorius because of its "estrogenicity", nor because of its lectins (9).

In Germany necklaces from India were sold in the seventies, but soon warnings were propagated because of toxicity of the components. Investigations resulted that they were made with Abrus precatorius beans and warnings were propagated (35). In Christian countries the beans are used for wreaths of roses (precatory beans), for necklaces and for ornamentals together with other flowers in garlands. In China the herb of A.precatorius is used as a folk-medicine for the treatment of bronchitis, laryngitis and hepatitis. Because of their platelet inhibiting activity

Results of experimental studies

abruquinones are supposed to be the active substances (13).

Pharmacological effects

Abrin is toxic not only in normal animal cells but highly toxic against tumor cells, too. Abrin suppresses the growth of solid Ehrlich ascites tumours, and fibrosarcoma in mice and rats (9).

Abrin from A.precatorius seeds after being purified on sepharose 4B affinity column brought significant reduction in tumor volume of mice and increased the life span of ascites tumour bearing mice. The effect was demonstrated in Dalton's Lymphoma ascites and Ehrlich's ascites Carcinoma cells after intraperitoneal administration. Prophylactic administration of abrin was found ineffective (29).

In cultured human cell lines, derived from acute lymphoblastic leukemia (ALL, Jurkat, CCRF-CEM, MOLT-4, and HPB-ALL) abrin A induces apoptosis. This process was dose - and time-dependent. It starts one hour after abrin A application. Its maximum is on the third or fourth hour and ends with DNA-fragmentation on the fourth or sixth hour, depending on the cell line used. There was a positive correlation between the agglutinating activity of abrin A, and the development of apoptosis till DNA fragmentation, finally. This suggests that the B-chain probably triggers the apoptosis, while the A-chain and breakage of the disulfide bond are responsible for its progress (24).

The abruquinones from the roots of A.precatorius exhibit remarkable effects on the platelet aggregation. The IC50 of abruquinone A and B for the inhibition of platelet aggregation in- duced by arachidonic acid and collagen are less than 5 μ g/ml that of abruquinone is less tha 10 μ g/ml. On the other hand, abruquinones A, B, D, F show strong antiinflammatory and and antiallergic effects (13).

Polymyxin B-induced hind-paw oedema was suppressed by abruquinone A in normal and as well in adrenalectomized mice, but it did not increase the liver glycogen content in fasting adrenalectomized mice. In neurogenic inflammation, the volume of exsuded plasma was significantly reduced by abruquinone A. Histamine-, serotoninand bradykin- induced plasma extravasations in the ear oedema were also suppressed by abruquinone A. These and further results suggest that the antiinflammatory effect of abruquinone A is mediated partly via the suppressed release of chemical mediators from the mast cells and partly via the prevention of vascular permeability changes caused by mediators (40).

According to the Igbo-Nigerian folk medicine evaporated alcoholic extracts are widely used in vaginal pessaries for abortion. A physical dispersion of seed oil was administred on guinea pig ileum. In concentrations less than 1.8 mg/ml there was no stimulation of the organ preparation but up from this value the twitches were enhanced. The contractions were resistent to atropin or indometacin, partially (22). The aqueous methanol extract from seeds of A.precatorius elicited a biphasic response on the field stimulated guinea-pig ileum, being inhibitory in low concentrations but excitatory in higher concentrations. The excitatory component contracted most smooth muscle including uterus. This action was atropine - sensitive. The inhibitory component also contracted the uterus but relaxed other smooth muscles. It could not be suppressed by common pharmacological blocking agents with the exception of indometacin which acts on smooth muscles. The two activities were separated by Sephadex gel filtration (23).

A substance BN prepared from seeds of A.precatorius by methanol-water reduced rhythmic contractions of guinea pig ileum. The same activity was found to be inhibitory for the frequency of de-faecation in rats with castor oil induced diarrhoea. The substance BN was found to be less potent than the standard antidiarrhoeal substance diphenoxylate (22).

Immunstimulatory effects

A simple method for determing cytoagglutination is measuring the turbidity of cell suspensions at 600 nm. Upon addition of abrin a to the cell suspension turbidity decreases at 600 nm. This change is proportional to the cytoagglutination curve. From

this the velocity and intensity of cytoagglutination can be measured, depending from different cell lines. Abrin B derived from seeds of A. precatorius causes a strong agglutination of cells. This agglutination increases according to the order of differentiation in cells (24).

Native and heat - denaturized agglutinin from seeds of A.precatorius alters the macrophage function of mice in vitro. Both substances are immunstimulants (38). A non toxic dose of abrin $(1,25\mu gram/kg body weight)$ can potentiate an immunresponse of a host, like increase in total leucocytes, weights of thymus and spleen (28).

The ethanol extract of leaves inhibites muscle preparations, like toad rectus abdominis and rat diaphragm. The effects were reversible and depending on the contraction. Comparing different extracts the authors believe that the poisonous component resides mainly in the ethanol extract (39).

Effects on snails

In India, the Abrus precatorius-components, abrin and glycyrrhizin were used against the snail Lymnaea acuminata. They cause a significant decrease in the levels of protein, free amino acids, DNA and RNA in the nervous tissue of Limnaea acuminata (32).

Antifertility activity

In an antifertility program three indigeneous plants (Piper longum, Lawsonia inermis and Abrus precatorius) were studied with pregnant rats. Between these plants Abrus precatorius was the most effective one. A daily dose of 3.30 or 300mg showed a 40 - 60 percent inhibition of pregnancy of rats (19).

A methanol extract of A.precatorius seeds impaired the motility of washed human spermatozoa with an EC 50 of 2.29 mg/ml, irreversibly. With the highest concentration tested (20.0 mg/ml), the onset of the motility was almost immediate. In contrast, this and other effects were not evident at a lower concentration than 5 mg/ml. Scientists from the University of Colombo, Sri Lanka confirm these results (31). Male albino rats treated with 50% methanol extract 250 mg/kg for 30 and 60 days became absolutely infertile. This was reversible. This treatment met the energy metabolism of the cauda epididymidis. Levels of acid phosphatase and succinic hydrogenase were significantly depleted, while protein and sialic acid appeared normal (33).

In a similar investigation male albino rats were treated with an alcoholic seed extract of A.precatorius at a dose of 100 mg/kg for 60 days. The data revealed that the cauda-epididymal sperm motility was significantly lowered. There was no effect in the sperm concentration by the 60 days of feeding. The electron microscopy on sperm morphology exhibited decapitation, acrosomal damage and bulges on midpiece region of sperm in treated rats. Energy metabolism altered by a fall in succinate dehydrogenase and ATPase activity by extract allocation. Contrarily a significant increase in serum testosterone levels was noted after 60 days of administration. The authors conclude that the decreased fertility rate is correlated with reduced sperm motility, and an altered sperm morphology in epididymis (30).

In testes of rats treated with the steroidal fraction of seeds of A.precatorius degenerative changes were observed, like in testicular weight, in sperm count and later stages of spermatogenesis and in Leydig cells. These are correlated with the dose-dependent decrease in enzyme activity of hydroxysteroid dehydrogenase, glucose-6-phosphatdehydrogenase, sorbitol deydrogenase, and leucin aminopeptidase. The

steroidal fraction may exert their influence indirectly by a feedback reaction decreasing the production and release of testosterone, additionally (34).

Results of clinical studies

All clinical reports are dealing with intoxications, in many cases with fatal outcomes!

Only one older report with positive efficacy can be reported from opthalmology in the nineteenth century. A French eye doctor observed that an extract of A.precatorius beans brought into an eye caused an inflammation followed by brightening of dimmed corneas, but this method was not used for longer time (6).

Toxicity

Abrus precatorius beans are known as ones of the most toxic plant parts worlwide.

If eaten, one or two beans only, there are reports of fatal outcomes with people. But swallowing of intact beans is nearly harmless, likewise eating of boiled seeds as some indigenous people do.

Abrin is the toxic protein obtained from the seeds of Abrus precatorius. In structure and properties it is similar to ricin. The human fatal dose is estimated as

$0.1-1 \mu g/kg$

At the cellular level abrins (a-d) inhibit protein synthesis by changing the enzymatic state of the subunit in the 60S-ribosome. The beginning of the cell damage consists of a abrin induced endothelial lesion, followed by an increase in capillary permeability with fluid and protein leakage and tissue oedema, the so called vascular leak syndrome. Abrus agglutinin causes a total haemolysis in all bloodgroups followed by a haemorrhagic gastroenteritis (6).

Most reported cases of human poisoning involve the ingestion of single jequirity beans, which predominantly causes gastrointestinal toxicity. In every case medical management is required. Only symptomatic and supportive treatment is known (4). The clinical features, reported here from the General Hospital in Kandy, Sri Lanka include pulmonary oedema and hypertension (5).

One case of jequirity bean ingestion and its management at Cardial Glennon Memorial Hospital for Children is reported in 1980 (11).

A report of poisoning by the white seed variety of A.precatorius bean was published in 2005. A middle aged male had consumed the seeds on the advice of a folk medicine practitioner. The patient recovered after a prolonged stay in a hospital without any subsequent complications (26).

One most difficult case of poisoning was reported from an Indian male in Hamburg, Germany. The patient suffering from gastroenteritis was brought into the hospital. Before this he had taken a probe from an Indian wholeness powder consisting of ground seeds of A.precatorius, against his illness. Then he was afflicted with diarrhoea, with pancreatitis, subileus and diabetes mellitus. Finally he became deeply unconscious and must be treated by a respiration machine. After 40 days he left the hospital with diabetes mellitus and not wholly correct liver enzymes (6). Eight Nubian **goats** were given A.precatorius seeds at 2.0 and 0.5 g/kg daily. Six goats receiving the seeds at 2 and 1g/kg died between days 2 and 5. One goat receiving the seeds at 0.5g/kg died on day 32 and the last one on day 33. The main signs of poisoning were inappetence, bloody diarrhoea, dyspnoea, dehydration, loss of

condition and recumbency. The lesions of the inner parts were fatty lesions and necrosis of hepatocytes, convoluted renal tubuli, pulmonary haemorrhage, oedema and emphysema and erosions of the intestinal epithelium. The accompanying enzyme defects were increases of GOT and gamma GT, increases of urea, creatinine, sodium, potassium and decreases of total protein and albumine in the serum. The blood cells showed haemoconcentration (2).

Evaluation

Because beans of A. precatorius belong to the most toxic plants all over the world all uses of every part of this plant must be advised against, emphatically.

Every advice for any application must be denied, therefore.

Abrus precatorius:

No positive evaluation

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