Working together to eliminate cyanide poisoning, konzo, tropical ataxic neuropathy (TAN) and neurolathyrism

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Editorial

With CCDNN21 we start the second decade of regular bi-annual publication. After a smooth transition in 2012, the newsletter is now published by an international editorial committee coordinated from Ghent University. With this issue we further extend the geographical coverage with contributions from China and India on aspects of neurolathyrism. A group from Australia and one from the US report on aspects of konzo in central Africa. These results support our hope that perhaps in another decade, konzo and neurolathyrism will disappear and only have historical importance. As a way to consolidate recent progress, an international "Cassava Cyanide Diseases Workshop" will be convened shortly, probably in Kinshasa, D.R. Congo. Detailed notifications will follow. We start with the abstract of a lecture presented at the 1st Legume Society Conference, 9-10 May 2013 in Novi Sad, Serbia.

Lathyrus sativus: To eat or not to eat?

In its long history as a cultivated crop, grass pea (*Lathyrus sativus* L.) has received praise and blame. In the Pharaonic era, grass pea was part of funeral offerings found in the pyramids. In drought prone areas of Ethiopia and the Indian Sub-continent, grass pea is considered a life-insurance crop. Already in antiquity, the link was made between overconsumption of grass pea seeds and a crippling neurological disorder, later coined neurolathyrism. Overemphasis on suspected toxicity of the seeds has led to neglect of the exceptional positive agronomic properties of the plant. In normal situations, neurolathyrism is virtually non-existent. The etiology of neurolathyrism had been oversimplified as being caused by a single metabolite and factors such as oxidative stress, mineral content, the total diet, emotional stress and deficiency of essential amino acids were neglected. Recent epidemiological and pharmacological studies have indicated the importance of essential amino acids and oxidative stress in the incidence of neurolathyrism. The same metabolite that is considered the cause of neurolathyrism is also present in Ginseng and patented in China as a haemostatic drug.

The drought tolerant grass pea is the survival food for the poor during drought-triggered famines. It is the most efficient nitrogen fixer among commercial legumes, grows on poor soil and yields even better in moderate salinity. Grass pea can become a wonder crop if it can shed the double stigma of being a toxic plant and the food for the poorest of the poor. All strategies including genetic transformation need to be exploited.

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Konzo control and cassava safety using the popular wetting method to remove poisonous cyanogens

Konzo is an irreversible paralysis of the legs that occurs mainly in children and young women after childbirth, associated with (1) a high intake of cyanogens from a monotonous diet of bitter cassava and (2) a diet that is deficient in protein, in particular the S-containing amino acids methionine and cysteine/cystine, that are needed to detoxify cyanide to produce thiocyanate.[1-3] Konzo is a non-progressive upper motor neuron disease of sudden onset that was first discovered by Trolli [4] in 1938 in Popokabaka Health Zone, Bandundu Province, Belgian Congo, now the Democratic Republic of Congo (DRC). A recent estimate of the number of konzo cases in the DRC was 100,000. Konzo also occurs in lesser amount in Mozambique, Tanzania, Cameroon, Central African Republic and was recently reported from

Angola.[5] It has been controlled for the first time ever, in the same Health Zone in which it was first discovered, by reducing greatly the intake of cyanogens from cassava flour.[6] The wetting method has now been shown to be a popular method to ensure food safety.[7]

The cyanogen content of cassava flour, prepared by traditional methods of soaking peeled roots in water or sun drying, is greatly reduced using the simple wetting method, as follows.[8-10] The flour is added to a bowl and the level marked on the inside of the bowl. Water is added with mixing until the level of the wet flour comes up to the mark. The wet flour is spread out on a mat in a thin layer and the enzyme (linamarase) breaks down the cyanogen (linamarin) to acetone cyanohydrin that hydrolyses spontaneously at about pH 6.5, liberating hydrogen cyanide (HCN) gas, which escapes from the sticky wet flour. The process requires about 2 hours in the sun or 5 hours in the shade for nearly complete removal of cyanogens.

The women in the village of Kay Kalenge were educated about the poison present in cassava flour and shown how to use the wetting method to remove it. They accepted the method and used it on their cassava flour. Monthly visits were made to the village by Sister Mandombi's Caritas team to help the women use the method correctly and every four months Dr Banea's full team visited the village to check on any new cases of konzo and measure the total cyanide content of flour samples just before they were used to prepare the thick porridge (fufu), which is eaten with something to give it flavour such as pounded, boiled cassava leaves.[11] Analysis of urine samples from school children for thiocyanate, produced by detoxification of ingested cyanide, gave a good measure of cyanide intake over previous days.

No new cases of konzo occurred in Kay Kalenge during the 18 month study, the total cyanide content of cassava flour samples fell to below the WHO safe level of 10 ppm and the urinary thiocyanate content of school children reduced to safe levels.[6] In 2011-2 we made a 12 month intervention in three villages in Boko Health Zone where there were 61 konzo cases and a mean prevalence rate of 4.6%. The intervention has proved to be just as successful as that in Kay Kalenge with no new cases of konzo occurring in the villages and large reductions in cassava flour cyanide and in urinary thiocyanate levels. Also the people of surrounding villages were willing to use the wetting method.[12] Another successful intervention in three more high prevalence konzo villages is nearing completion also with AusAID support.

We returned to Kay Kalenge village 14 months after the intervention ceased. We were pleased to find that there were no new cases of konzo in the village, all the women were still using the wetting method and the total cyanide content of flour samples and urinary thiocyanate levels were low. But most pleasing was the fact that the wetting method had spread by word of mouth to three nearby villages.[7]

Why is the wetting method so popular with rural women? Because it is simple and does not require much extra work or additional equipment, except for a basin and a mat. The treated flour produces high quality good tasting fufu, because of removal of the bitter taste of linamarin, and the fufu can be stored for up to three days.[6,13] Most importantly, it ensures food safety. It has been shown that high cyanide intake from cassava at levels not sufficient to cause konzo, is associated with impaired intellectual development in children.[14] To avoid this undesirable effect on their children, many families in tropical Africa and elsewhere who consume cassava flour may wish to use the wetting method to ensure food safety.

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The cultivation, consumption and research progress of *Lathyrus* in China

Grass pea (*Lathyrus sativus* L.), also named horse-tooth-like pea, three-edge pea or *song liu* pea since its leaves are similar to the ones of pine and willow in China, is an annual pulse crop belonging to the family *Fabaceae* and the tribe *Vicieae.* It has been cultivated in China for over 600 years according to historic records. During the famine times grass pea used to be the only lifesaving food for both human consumption and animal feeding. At present, grass pea has been extensively cultivated and naturalized as a forage crop in fields with different soil types. Here, we mainly report on the cultivation, consumption and research progress of grass pea in China.

The cultivation history and current status of grass pea

The cultivation of *Lathyrus* species in China has a long history, the earliest historical evidence comes from the *Jiu Huang Ben Cao* (on wild food plants for use in emergency) by Su Zhu in the early Ming dynasty (about 1400s). Nowadays, the main *Lathyrus* species cultivated in China are *L. sativus*, *L. cicera*, *L. odoratus*, *L. tingitanus* and *L. quinquenervius.*[1,2] Among them, *L. sativus has* a wide range of cultivation in the northeast, northwest and southwest of China. In the 1960s, Chinese people suffered from a severe grain deficiency due to drought and many other reasons. As a result grass pea was over-consumed as an exclusive staple food, especially in the low-income and food deficit areas, which led to the occurrence of serious neurolathyrism. Therefore, grass pea was forbidden by the government to be consumed as food in the 1970s. In spite of this, grass pea is still cultivated for animal forage, especially in the northwest of China[3,4] and Inner Mongolia.[5] Dingxi region in Gansu province, including one administrative area and six counties, is the main cultivating area for grass pea in China, producing approximate 5000 tons of seeds in 2012,[7] occupying 3.3% of the total forage area for its abundant nutrients,[6] and the yield of grass seeds is about 1.13 ton per hectare.

The consumption of grass pea and neurolathyrism

In addition to the extensive use of its seeds as forage, grass pea seedlings are also utilized as a potherb.[8] At present, Chinese people usually prepare it for consumption by baking the seeds, stir-frying or boiling soup using its sprouts mixed with other foods, like eggs, meat and shrimp or other vegetables. Recently, a research group reported that the seedlings of grass pea which is called grass pea sprouts could be eaten as either cold dishes or hot pot vegetables.[9] We have investigated 15 large supermarkets in Lanzhou, and found 4 supermarkets selling grass pea sprouts provided by special producers, however, the amount of sales is quite small. Moreover, *L. quinquenervius* is now used as a precious herbal medicine in the northeast of China for its effectiveness in treating arthritis and headaches. A recent study has reported the value of grass pea as a green manure for improving soil nutrients.[10]

According to the records of Gansu Provincial Archives, neurolathyrism occurred in 8 counties in the 1970s, including Gangu, Qin'an, Longxi, Hoeryong, Tongwei, Wushan, Yuzhong and

Tianshui and was caused by excessive consumption of grass pea. A total of 2315 cases of neurolathyrism were identified in these areas. The main symptoms of neurolathyrism are dizziness, headache, lacking of energy, lassitude and nausea, further development of the disease could cause lower limb numbness and weakness, leg twitching, trembling and stiffness. In severe cases patients walk becomes difficult with scissor gait. Of all the cases, 85.6% were man, aged from 18 to 40, and 204 cases were bedridden. In the 1990s, Gansu Provincial Hospital also surveyed neurolathyrism in the outbreak areas which were linked with poverty and illiteracy. After neurologic examination of 2128 farmers, 119 were diagnosed to have neurolathyrism, accounting for a prevalence of 5.6%. The diagnosed patients consisted of 95 men and 24 women, among them 65 were hard laborers, accounting for 7.9% of the total labor forces. Clinical researches revealed that the motor neuron injury of neurolathyrism was related to prolonged overconsumption of grass pea, and the more severe symptoms was related to the higher proportion of grass pea in staple food. Additionally, neurolathyrism could be easily prompted in high humidity and cold environment. A followed-up study 24 neurolathyrism sufferers for 23 years demonstrated that none of them recovered.[11]

The research progress of grass pea in China

Since grass pea has a long history of cultivation as food for human consumption and feed for animal stock, it has been continuously researched and was found to be superior in many quality parameters such as strong resistance, nutritional value and nitrogen fixation. Current researches of grass pea in China are focused mainly on following six areas:

(1) *The extraction and detection of β-ODAP*. Zhang et al[12] have developed a method to analyze β-ODAP and its inactive isomer α-ODAP using 2,4-dinitrofluorobenzene (DNFB) for precolumn derivatization. Jiao et al[13] have successfully separated β-ODAP in grass pea by thin layer chromatography. Zhao et al[14] used pure water, 30% aqueous ethanol and 0.2 mol/L perchloric acid to extract β-ODAP and found that 0.2 mol/L perchloric acid extraction combined with HPLC (high performance liquid chromatography) is an optimized method.

(2) *The screening of low toxin varieties*. Numerous works have been done to select low toxin varieties of grass pea. Bao et al[15] have selected three varieties with higher yield and protein content and lower content of toxin from 65 varieties during three years. The mutagenic effect of heavy ion C^{6+} on the dry seed of grass pea has been studied by Wang et al,[16] who discussed the suitable dose of C^{6+} for inducing low- or non-toxin genotypes of grass pea. Chinese researchers found that the processing of grass pea to vermicelli can dramatically decrease the content of β-ODAP to less than 1%.[17] In addition, both microbial fementation[18] and two successive solid state fermentations[19] could reduce the neurotoxin β-ODAP efficiently.

(3) *Investigation on the biological significance of β-ODAP*. β-ODAP was also discovered in the well-known traditional Chinese medicinal herb *Panax notoginseng*, in which it was named dencichine and used as a haemostatic.[20] Although β-ODAP can lead to neurolathyrism, it had no influence on animal reproduction. Feeding animals with enormous amount of grass pea for long term could not cause cancer or trigger tumour.[21] Since the high level of β-ODAP and excellent drought resistance simultaneously exist in grass pea, Xing et al[22,23] put forward an assumption: the function of ODAP may be similar to polyamine and proline under stress condition, because ODAP is not only a nitrogen compounds, but also a free amino acid and soluble in water, which can be regarded as osmotic regulation substance and an agent preventing dehydration to play an important role in nitrogen and energy metabolism. It provides a novel idea to study the drought resistance of grass pea.

(4) *The factors influencing β-ODAP content*. There were different levels of β-ODAP at different developmental stages, and the young leaves and mature seeds contain the highest level of β-ODAP.

Field studies have shown that β-ODAP levels in seeds were correlated positively with P, and negatively with Zn, N, Ca, K or Mg in the soil, and the level of β-ODAP in seedlings obviously reduced when infected by *Rhizobium*. It was also found that drought stress could increase the levels of β-ODAP in the seeds. In addition, β-ODAP accumulation could be related to low levels of endogenous H_2O_2 in the leaves under either field conditions or osmotic stress.[24]

(5) *Studies on drought resistance*. Sun et al[25] treated *L. sativus* seedlings with PEG6000 to explore the physiological mechanism. Through a series of experiments, they suggested that the seedlings of *L. sativus* could alleviate its stress damage by the reduction of stomatal conductance/transpiration rate and the increased accumulation of proline, which might be a drought resistant mechanism. Jiang et al[26] also certified that the accumulation of osmoprotectants and the improvement of oxidation resistance resulted in the higher drought tolerance of grass pea compared to pea. Tian et al[27] have shown that Eu^{3+} induces abscisic acid early and promotes accumulation of ABA in grass pea under drought stress. In order to further explore the drought resistance mechanism of grass pea, Wu et al[28] established two-dimensional electrophoresis of leaf proteins of *L. sativus*, which lay the foundation for further proteomics research. Meanwhile, a recent finding[29] indicated that the peroxidase activity of grass pea becomes higher than in the control when treated with Cu^{2+}. Moreover, the level of reactive oxygen species (ROS) in grass pea increased significantly when it suffered from drought stress, and reduced glutathione (GSH) plays an essential role in ROS balancing, therefore it acts as an important molecule in the drought resistance of grass pea. Yang et al[30] developed fluorescence spectrophotometry for measurement of GSH in grass pea tissues, which contributed to the studies for resistance mechanisms of grass pea.

(6) *On other aspects*: Jiang et al[31] found that exogenous hydrogen peroxide reversibly inhibited root gravitropism and induced horizontal curvature of primary root during grass pea germination. Xu Shanshan[32] explored the optimal condition to extract protein from *L. sativus*. Zhang et al[33] optimized the extracting conditions of *grass pea* starch, which combined immersion method with protein enzymolysis using Alkaline protease. Ecological studies on grass pea were mainly focused on the growth and development regularity, floral dynamics and breeding system of *L. qinquenervius*, and its community ecology.[34,35,36]

Although grass pea has a number of unique features that make it attractive to the grower and consumer, there are still plenty of works that remain to be done: ⅰ) Most people know little about grass pea so that they buy and consume grass pea seedlings in their daily life unwittingly. Therefore dietary information, education, and communication on safe grass-pea preparations should be developed. ⅱ) With regard to the screening of low-toxin grass pea species, molecular biological technique should be used to produce new grass pea genotypes which are safe for human consumption. ⅲ) Meanwhile, grass pea is an efficient nitrogen fixer and is also a very intensively nodulated legume and studies on its nitrogen fixation process will provide new insights into its cultivation. ⅳ) The role of ODAP in the resistance to various abiotic stresses and nitrogen fixation of grass pea needs to be further explored. ⅴ) Moreover, the medicinal value of grass pea is also worthy to be further investigated.

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Impact of cross-sectoral approach to addressing konzo in DRC

Introduction

From December 2009 to October 2011, Action Against Hunger (ACF-USA) implemented an intervention in the Bandundu province of the Democratic Republic of Congo (DRC) addressing factors underlying the konzo epidemic affecting the population of Kwango district. The 'Integrated Programme for the Eradication of Konzo in the Territory of Kwango in DRC' project was financed by the European Union (EU) Food Facility and aimed to eradicate the disease through a cross-sectoral approach focused on nutrition education and training, dietary diversification, improved water access and agricultural processing. The strategy also aimed to address the high rates of malnutrition seen in konzo cases (25.8% global acute malnutrition (GAM) prevalence in konzo affected children less than 18 years old, 69.3% of GAM in konzo affected adults). A total of 22,000 households benefited from these activities. The project was implemented in 396 villages in the highly affected areas of Kahemba, Kajiji, Feshi and Panzi and to a lesser extent in Kenge, Boko, Popokabaka, Kasongo Lunda, Wamba Luadi and Kitenda across the Territory of Kwango. Due to limited resources, project activities were not carried out in all konzo locations, but rather in the most affected villages.

Konzo is a sudden epidemic spastic paraparesis (paralytic) disease which leads to a permanent paralysis of the affected person's lower limbs. It is a neurological ailment triggered by sustained dietary exposure to cyanide present in improperly processed cassava. Overall, vulnerability to konzo is heightened by the combination of low protein intake (associated with low dietary diversity), poor soil conditions (which favour the cultivation and consumption of bitter cassava varieties high in cyanide), and lack of sufficient water resources for thorough processing.

Methods

The impact study was conducted across the area targeted by the project. A stratified sampling approach was used, with six of eleven intervention health zones selected purposively and 40 of 395 intervention villages selected randomly. In each selected village, six beneficiary households were randomly selected to participate in household surveys (234 in total). Household surveys were supplemented with information from key informants and focus groups.

Findings

Knowledge and attitudes on konzo and nutrition

ACF employed a community outreach and mobilisation approach through the creation of community cells as a forum for discussion on konzo and nutrition. These served as launch pads for a broadly based educational campaign which extended to churches, schools, training of local health professionals, community volunteers and leaders, traditional authorities, etc. Changes in knowledge at endline compared to baseline suggest that community outreach and education activities were effective in challenging long held local beliefs on konzo and nutrition. At project baseline, 74% of sampled population attributed the disease to a metaphysical origin, while 88% correctly noted the food-related causes of konzo at endline. Similar results were found regarding knowledge, attitudes and practice on prevention strategies based on effective messaging that encouraged appropriate processing of cassava and inclusion of protein in diets through incorporation of maize flour into *fufu* preparation and legumes (pulses) in the diet.

Food stocks and dietary diversification

ACF introduced two improved food crop varieties, *niébé* (cowpea) varieties *Vita 7* and *Muyaya,* and sweet cassava varieties *TME119, Mwuazi, Nsasi, Disanka* and *Butamu* to support increased consumption of sulphur amino acids methionine and cysteine contained in cereal and leguminous foods and complement consumption of traditional cyanide-heavy bitter cassava varieties with varieties low in cyanide. Notable improvement was seen in overall food stocks and diversity of food items held by households over the life of the project. The positive trend in diversity and volume of household food stocks may be attributed to project impact, in particular IEC activities around balanced diets and food processing and preparation, as well as external factors such as climate, crop disease and seasonal fluctuations.

Cassava retting techniques and water access

ACF also supported the installation of village based mills to increase access to maize and cassava milling services and improve the quality of the flour. Finally, ACF implemented a variety of hydraulic constructions: public retting tanks to process cassava, boreholes, springs, rainwater harvesting systems and piped distribution networks. Knowledge of community leaders and member households of community cells regarding cassava retting and drying techniques similarly improved. Community leaders correctly reporting optimal processing time increased from 60% to 99%. Member households showed similar improvement of knowledge but constraints around access to processing sites and water quality limited optimal practice. At endline, a majority of households indicated they were processing cassava in rivers or ponds and had largely abandoned utilization of home retting techniques that rely on prolonged use of the same water, saturated in acid and less effective in cyanide detoxification.

Konzo incidence

Kahemba health zone was found to harbour the highest number of confirmed cases at project baseline (1,639), and placed among the top three zones for incidence (2.08%) largely due to its density of population and associated risk factors. A surveillance system for screening and identification of konzo cases in Kahemba health zone was established by the local health structure in 2009, with annual caseload an estimated 1,300 individuals in 2009. MoH educational activities and ACF integrated activities on konzo were launched in early to mid 2010, with a marked decrease in cases recorded that year. A further reduction in caseload between 2010 and 2011 was noted during the critical months of June, July and August with 47 new cases recorded in 2011, an 84% reduction in annual incidence. The greatest reduction in new cases was observed among the under 5 years age group.

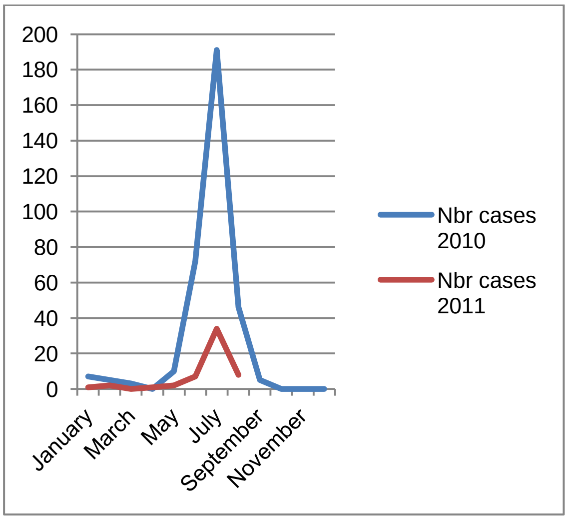

Figure 1: Comparison of number of konzo cases in Kahemba health zone in 2010 and 2011

Conclusion

ACF's multi-tiered community outreach and education strategy proved effective in the dissemination of information on a large scale. The community cell approach allowed for a deep, sustained and broad based appropriation of messages and activities around nutrition education and konzo that would not otherwise have been possible.

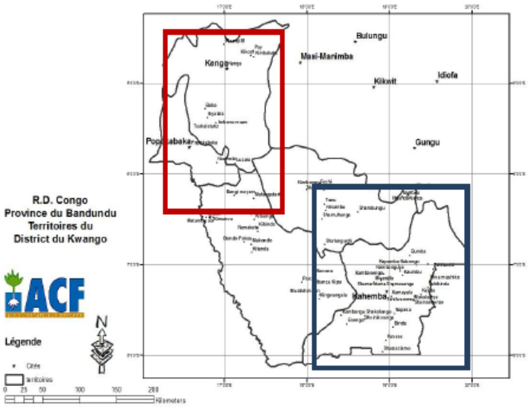

Figure 2: ACF program area in Kwango district, Bandundu province, DRC

Placing community members in leadership positions to carry out sensitisation allowed local taboos to be effectively mitigated through open discussion. This approach also permitted the affected population to control the educational process, encouraging better appropriation of messages, knowledge transfer and behaviour change. Impacts achieved through the community outreach and education approach were reinforced by improved access to water, agricultural processing infrastructure and opportunities to diversify diets.

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Further reading:

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For more information or to receive the full French language study report, contact: Muriel Calo, email: mcalo@actionagainsthunger.org

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Safety and toxicity profile of grass pea (*Khesari dal*): A reappraisal in the Indian scenario

The disease Neurolathyrism has gradually disappeared over the past three decades from India in particular and may soon become a part of history and even our views on grass pea (*Khesari dal, Lathyrus sativus*) toxicity have seen paradigm shifts. Neurolathyrism is now recognized as a disease that results only following excessive consumption of the pulse as a staple for prolonged periods especially under drought and famine situations wherein it is also the only survival food for more than 98% of the population. *Khesari dal* cultivation continues in several parts of India without any adverse effects reported during the last three decades. Recently some states in India have even revoked the ban on its sale. Some of these developments thus necessitate a reappraisal especially in the context of several recent developments and also lessons learnt from the Ethiopian incidence.[1,2] This brief review is to highlight some of the more important features that need to be considered in this regard.

Homoarginine (HA) the first unusual amino acid characterized from grass pea has over the years gone into the background as it had no toxic attributes. However, HA is now recognized as a normal metabolite in humans and its importance in human health is growing.[3,4] HA is a better substrate for Nitric oxide synthase (NOS) compared to arginine and could be a source of sustained generation of NO.[5] The health benefits of NO both for the cardiovasculature and cerebral metabolism are now universally recognized. HA is also a weak inhibitor of arginase and may contribute to a raise in arginine levels.[6] This is evidenced by the increased nitrate excretion in individuals on a grass pea diet. NO is a "master signaling molecule" and its role in cardiovascular physiology and health are very well established. A daily intake or supplementation with *khesari dal* may be of an added advantage due to its HA content and make it an unique and prized functional food as it could have a vasodilator effect and prevent prehypertension from progressing to full blown hypertension, a major risk factor for heart attacks and strokes. Recent clinical studies do show that higher HA levels are associated with lowered blood pressure and a higher survival rate from cardiovascular events. Some genetic information suggests that lowered HA levels due to the deficiency of arginine glycine amidinotransferase (AGAT) may be the link to the pathological basis of acute ischemic stroke.[7]

New research also suggests that HA may be important for skeletal health and its deficiency may be associated with high bone turnover and low bone mineral density (BMD)[8]. This property may be related to the weak inhibitory effect of HA on alkaline phosphatase[9]. HA is also an inhibitor of glycine uptake at the synapse (Author *unpublished results*) and this may benefit LTP, one of the major cellular mechanisms that underlie learning and memory. Unlike arginine, HA is not a substrate for pancreatic arginase and thus may be a better insulin secretagogue compared to arginine.[10]

Much of the research on grass pea toxicity has always centered on ODAP, and its acute toxicity is now well demonstrated. Primate model studies have had some success but only under intrathecal or lumbar routes of ODAP administration or oral feeding of large quantities of the seeds, seed extracts or fortified seed extracts and complex feeding regimens.[11,12] In humans much of the ingested ODAP is metabolized (detoxified) and very little of it is excreted in the urine (less than 2% in 24 hrs) while in rats, chicks or monkeys at least 95% of ODAP is excreted unchanged which suggests that humans have a unique ability to metabolize (oxidation?) ODAP.[13]

Some recent studies show that ODAP is a nonapoptotic activator of PKC followed by several downstream events which includes stabilization of HIF and expression of VEGF and eNOS.[14,15,16] Some of these findings provide fresh leads into possible therapeutic applications of both ODAP and HA and utilization of grass pea for human health. The discovery of ODAP (Dencichin) as a constituent of *Panax Notoginseng* the traditional Chinese medicinal herb is a new twist to the ODAP and grass pea saga.[17] Several of the curative attributes of this herb are now ascribed to its Dencichin (ODAP) content. Some of the attributes of ODAP (Dencichin) are now being explored for potential therapeutic applications. Some therapeutic applications of ODAP/Dencichin that have been patented very recently are a) US patent for its application as a hemostatic agent[18] b) China patent for the Fourth Military Medical University for its use in preparing a medicament for treating neurodegenerative diseases[19] and c) China patent for its use in toothpastes to prevent oral ulcers (98% efficacy) and for dental hygiene.[20] More patents based on use of ODAP in combating Hypoxia, stroke and other applications are very likely in the future.

All the surveys done during the last 60-70 years with grass pea consuming cohorts have only focused on the incidence of neurolathyrism and finally we have only realized that it is a simple case of excessive consumption of grass pea as a staple for many years that is the root cause. The time has now come to change this approach and what is now needed is to give up the conventional reflex hammer approach but identify the positive contributions and effects that grass pea can offer.

A whole new approach is now possible with the newer inputs on ODAP and HA. It seems appropriate at this stage to ponder if grass pea consumption as part of a cereal based diet is fit as a functional food until we are able to fix its daily dietary intake limits and this would be the way to move forward to restore its deserved place in human health and nutrition.

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