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

CCDN News

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CCDNN Coordination:
Prof Fernand LAMBEIN, Coordinator
Ghent University, Institute for plant Biotechnology Outreach (IPBO)
Technologiepark 3, B-9052 Gent-Zwijnaarde, Belgium
Phone: +32 484 417 5005
E-mail: Fernand.Lambein@ugent.be or Fernand.Lambein@gmail.com

Dr. Delphin DIASOLUA NGUDI
Ghent University, Institute for plant Biotechnology Outreach (IPBO)
Technologiepark 3, B-9052 Gent-Zwijnaarde, Belgium
Phone: +32 92 64 52 82
Email: ddiasolu@yahoo.com

Country Contacts:
Cameroon: E.E. Agbor;
D.R. Congo: D. Diasolua Ngudi and J; Nsimire Chabwine;
Indonesia: A. Hidayat;
Mozambique: Anabela Zacarias;
Nigeria: M.N. Adindu and P.N. Okafor

Website: www.anu.edu.au/BoZo/CCDN (temporarily)
http://www.ugent.be/we/genetics/ipbo/en/networking/ccdnn/overview.htm

Announcements

GLOBAL ADVOCACY WORKSHOP: Brain Research, Nutritional Policy, and Programs for Child Development

September 4 and 5, 2014,

Kinshasa, Democratic Republic of Congo (DRC)

***Venue**: Hotel Sultani, Kinshasa, DRC*

In many parts of the world neurological diseases such as epilepsy, konzo, or neurolathyrism are not well understood or even accepted as major causes of disability. It is important that the public – from politicians and policy-makers to parents and children – be informed about the importance of brain research and how it can help provide a cure or at least alleviate the symptoms of neurological diseases. As Pierre Magistretti the President of IBRO said "With effective advocacy, greater political will and enhanced global cooperation, neuroscience will make faster progress for the benefit of all humans". Neuroscience research is the key to widening what humankind has already achieved with our brains, to secure a sustainable future for forthcoming generations as stated by the IBRO Global Advocacy Committee.

It is commonly accepted that most universities are founded with a civic purpose. Most donors expect changes in people's lives. We therefore have a fundamental obligation to apply our skills, resources, and energy to address the most challenging issues in our society.

Scientists from Africa, Diaspora, and Western Hemisphere will gather September 4 and 5 for the first workshop on Global Advocacy: Brain Research, Nutritional Policy, and Programs for Child Development, Kinshasa (DRC). Parallel activities include two-week long neuroscience teaching workshops for young African scientists.

Participants at the workshop are encouraged to seek their own funding to attend the workshop.

Contacts:

For any specific interest on attending the Konzo symposium, please contact directly

Jean-Pierre Banea, MD, PhD (Director Programme National de Nutrition, DR Congo); e-mail: jpbanea@pronanut.org;

or

Desire Tshala-Katumbay, MD PhD (Nutrition Toxicity Research); e-mail: tshalad@ohsu.edu

Participants who contribute lectures or communications on konzo related topics can submit abstracts to the editor for publication in CCDNNews

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SUMMER COURSE: Modern Breeding Techniques of Cassava

The Institute of Plant Biotechnology Outreach (IPBO – VIB/Ghent University) is organizing an advanced course "Modern Breeding techniques of Cassava" at Ghent University (Belgium) from 8 till 19 September 2014.

This course is aimed at training students and scientists from the public and industrial sector, who are involved in local breeding programs of cassava plants. During this two week course the major topics in the field of modern breeding, including the latest breeding techniques using molecular analyses as a tool will be discussed. The course will cover different kinds of markers and their use in breeding programs for fingerprinting, mapping of traits and QTL's, incrossing of specific genes (wild or transgene into cultivars) and quality assessment. The challenges to commercialize 'elite transgenic events' as well as legal issues related to plant breeding, such as breeders rights, will be discussed. In addition, a session will be organized on Cassava value chains to link advances in plant breeding with crop improvement objectives that are relevant for socio-economic impact.

The program also includes a day of practical exercises on molecular markers to familiarize participants with the associated lab techniques as well as excursions to crop processing plants.

A number of scholarships with support from VLIR-UOS for accommodation and travel expenses are available.

For more information on the program, registration, scholarship eligibility criteria and application forms, visit http://www.ugent.be/we/genetics/ipbo/en/education/summercourses/advanced-course-modern-breeding-techniques-of-cassava

Registrations are open till June 15th 2014.

contact: ine.pertry@vib-ugent.be

Articles

Crippling konzo in DRC, three generations later

A limited community study was conducted in Popokabaka, Kwango district in D.R. Congo where konzo was first reported three generations ago[1]. Poverty of the population, unsafe water sources, recrudescence of endemic pathologies and poor quality of the soil are among the problems encountered in this region.

Konzo is a non-progressive irreversible spastic paraparesis with sudden onset that can lead to complete dependency. This disease is associated with high dietary cyanogen exposure from insufficiently processed cassava roots. Ingested cyanogen is hydrolyzed enzymatically in the intestinal tract and the resulting HCN is then converted enzymaticaly by rhodanase into SCN^-, a less toxic metabolite that is excreted with the urine. This last detoxification reaction uses sulfur originating from dietary sulfur containing amino acids. Low intake of sulfur amino acids (methionine and cysteine) is suggested to be associated with increased risk for konzo in the high exposure regions. We assessed the prevalence of konzo, the household risk and protective factors, and the dietary pattern in four health areas, with together 12416 inhabitants in Popokabaka, Bandundu province, D.R. Congo. Those areas were pooled in two groups on the basis of the prevalence found and the incidence in the area was used to measure the risk of konzo.

487 heads or delegates of household selected randomly were interviewed and WHO criteria[2] was applied to detect or to confirm cases of konzo in the household. The illiteracy rate among the participants was 43 % and among the literate more than 50 % did not finish the primary school (sixth grade). About 75% of the female participants were illiterate and almost all of them were small-holder farmer. The incidence of konzo was significantly associated with the female gender ($P = 0.024$) and with unmarried status ($P = 0.030$). Women are most at risk for konzo and they play the primary role in the household food security. The lower education of these women seems to entail a higher risk for developing konzo in the family.

Among the 3015 individuals in the selected 487 households, 43 cases of konzo with onset from 1980 to 2002, were detected in 33 households. Although konzo was reported in this area in 1938[1], we found no cases with onset before 1980. No reports on the life expectancy of konzo patients were found. Konzo is still occurring in this area with an incidence of 1.3 ‰ in 2002. Female patients are predominant with a female to male ratio of 3.3:1. The mild form of the disease with reduced mobility was the most common (74 %).

The food consumption pattern of the selected households in both areas is dominated by cassava. Luku or fufu, a stiff porridge prepared by heating the cassava root flour with minimal water, was the main staple food consumed at least once a day in 99.2 % of households and the pounded cassava leaves (saka-saka) was the main side-dish consumed with luku in 40 % of households. Cowpeas (30 %) and sesame (23.2 %) were the other popular side dishes consumed with luku. Consumption of cereals ($P < 0.0005$) and sesame ($P < 0.0005$) were found to be protective factors against konzo. Similar protection by methionine-rich cereals was also found for neurolathyrism[3]. Mixing cassava with cereals, or with legumes such as cowpeas and cereals thus increase the quality of the meal by optimizing the balance of essential amino acids. Consumption of luku without addition of cereals was associated with increased incidence of konzo ($P = 0.010$). Consumption of raw sweet (?) cassava tuber ($P = 0.006$) is also found to increase the risk for konzo, while consumption of raw bitter cassava can give acute intoxication and even death. The diets in neurolathyrism prone areas (mainly grass pea or *Lathyrus sativus*) and in Konzo prone areas (mainly cassava or *Manihot esculenta*) are both deficient in sulfur amino acids[4]. Cassava roots or grass pea seeds are the cheapest food available in konzo endemic areas respectively neurolathyrism endemic areas. For resource poor subsistence farmers, avoiding the consumption of cassava roots or grass pea seeds is no option.

Cassava roots contain cyanogenic glycosides that should be removed by processing; peeling and boiling are not enough to lower the toxin to a safe level. The peeled roots need to be soaked in running water (retting or "rouissage"). Consumption of cassava soaked less than 3 nights was associated with increased incidence of konzo ($P < 0.0005$).

Culture and consumption of cereals, sesame and pumpkin seed should be promoted to increase the availability of sulfur amino acids in the diet. Appropriate information, communication and training in cassava processing have to be provided, and promotion of a better balanced diet may prevent this irreversible crippling disease konzo.

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D Diasolua Ngudi[1], JP Banea Mayambu[2] and F Lambein[1]

[1]IPBO, Ghent University, Belgium

[2]PRONANUT, Ministère de la Santé, D. R. Congo

The Socioeconomic and Neurological Burden of Neurolathyrism in Ethiopia – *the saga continues.*

Brief historical review

Around 10,000 years ago, humankind passed through a fundamental demographic evolution known as the Neolithic Demographic Transition (NDT); notably, the NDT was characterized by humans shifting from hunter-gatherer, foraging, and nomadic way of life to begin agrarian lifestyle composed of societal formations and land tenure systems[1, 2]. Agricultural adaptation promoted sedentary cultivation and domestication of selected plant and animal species within larger and denser population settlements. Agrarian way of life continued to promote reliance on farming and pastoralism which depended on availability of rainfall; this resulted in unexpected periods of crop and animal product failures which led to nutritional stress and search for crops that are resistant to dry seasons and monsoon periods[1, 2]. Farming was not merely impacted by natural forces of weather, but also by man-made dynamics within growing and dense populations with potentials of civil strife and discontent. As prime lands reached their maximum capacity, different factors led to exploration for secondary and marginal farming lands and thereof crops that could adapt harsher farming environments. By virtue of its high protein value, high calorie content, high crop yield, high nitrogen-fixing qualities (helping crop rotation practices), high forage value, resistance to biotic (e.g. plant diseases) and abiotic (e.g. dry and flood seasons) farming stresses, and being an important cash crop, the grass pea species of *Lathyrus sativus* is among the earliest primary domesticates of plant types selected for farming purposes[3, 4].

Scientific, clinical, and epidemiological relevance

The grass pea is currently deemed to be a model crop for sustainable agricultural development for the above-mentioned factors[4]. However so, its agricultural importance has been impacted by its association with a nutritional neurotoxicity known to mankind i.e. neurolathyrism[5]. A non-protein amino acid known as oxalyldiaminopropionic acid (ODAP) with is a structural analogue of the neurotransmitter glutamate is the neurotoxin which has been held responsible for motor neuron diseases resulting in degeneration of the long corticospinal motor tracts in neurolathyrism[5,6] . Epidemiologically, neurolathyrism usually occurred in epidemics rather than sporadic incidences; epidemics of often sudden onset spastic paraparesis happened around the world at different times[5, 7]. During epidemics, lathyrism also affects domesticated and farm animals such as horses and cattle, further worsening its burden[8]. There only exist six human pathology descriptions which further limit the clear understanding of aethiopathogenesis in neurolathyrism[9]. Coupled with the lack of pure animal models, the disease still leaves different questions unanswered – such as its preponderance of affliction among men, its clinical phenotype spectrum involving varying from pure motor to mild sensory and absence of sphincter problems, whether it is a multi-factorial illness where not only ODAP but also deficiency of other nutrients play important role, and whether there is genetic predisposition[5].

Lathyrus sativus: the *guaya* story - burden, challenges, opportunities in Ethiopia

The Ethiopian economy is largely agriculture-based; sustainable industrial-based economy is in its initiation phase. The grass pea (locally known as '*guaya*' in Ethiopia) is deemed to be an important part of the Ethiopian agriculture and agroeconomics for different reasons ranging from its peculiar adaptability to terrace highland farming, its resistance to waterlogging, dry seasons, and low soil fertility[10]. The grass pea accounts for nearly 10 % of the annual acreage of all pulses farmed in the country[11]; in terms of production and importance for farming economy, it is placed as the fifth most important pulse following faba bean (*Vicia faba*), field pea (*Pisum sativum*), haricot bean (*Phaseolus vulgaris*) and chickpea (*Cicer arietinum*)[10, 11]. Despite the problem caused by the neurotoxin ODAP, the area for grass pea cultivation has increased over the last 6 years, exceeding the total area occupied by the highly expensive pulse crop, lentil (Figure 1)[10, 11]. It is also projected that grass pea cultivation will increase in the near future along with climate change. Grass pea can grow in dry areas of 380-650 mm average annual rainfall to areas with rain downpour of 1300mm average annual rainfall[10]. The plant is also well-adapted to grow in the farming highlands of Ethiopia as high as 3000 metre above sea level[10]. The type of soil where grass pea is grown in Ethiopia is known as vertisol; vertisols have a natural vegetation of grassland, savanna, or grassy woodland known to have high content of expansive self-mulching clay known as montmorillonite that forms deep cracks in drier seasons or years[10, 12]. Grass pea grown on heavy soils, such as the Ethiopian vertisols, which have low levels of zinc and high iron content, also showed higher than average levels of the neurotoxin[10, 12]. The content of ODAP in grass pea plants grown under water deficit conditions is much higher than that of plants grown in wet conditions[12]. The plant tends to synthesize more ODAP when stressed by drier weather conditions than when it is growing under optimum conditions; this is one of the reasons which hindered the lasting utility of breeding seeds with low/no and stable toxin[10, 12]. At this juncture, it will also be useful to study whether exposure to higher water amount as in the case of rainy monsoons and waterlogging also stresses the grass pea to render it synthesize higher ODAP content.

Studies have shown the ODAP content of the different genotypes at various locations in Ethiopia to range from 0.051% to 0.392% at Debre Zeit, 0.163–0.328% at Alem Tena (drier site), 0.098–0.327% at Denbi and 0.075–0.344% at Akaki[10]. Even though some improvement in ODAP content has been achieved through breeding locally, most of the newly bred varieties with low toxin traits were unable to retain their low level of ODAP content when tested longitudinally. Interaction between genotype and environment impacts ODAP content, this is a recognized challenge which limited the application of the genetic results gained. A study in Ethiopia has shown the low prevalence of neurolathyrism among a community surrounding a lake, whose diet is supplemented by local fishery – as compared to an area far from fishing lakes, while compared communities were both exposed and were consuming similar amounts of the lathyrus[13]. Soaking the seeds in limewater overnight and boiling for two hours are among some methods which have been studied to have lower level of toxicity burden[14-16]. An Ethiopian study has compared level of toxicities between cooking using metal and clay utensils, the latter was found to have lower neurotoxin levels owing to higher iron oxidation and thereof free radicals generation in the former[13]. These studies indicate the importance of focusing on multifactorial ethiopathogenesis of neurolathyrism, and structure management and prevention plans based on such multipronged approach.

Safe ODAP level in grass pea seeds: is there such a threshold?

Grass pea seeds contain 18.2–34.6% protein, 0.6% fat, 58.2% carbohydrate (about 35% starch) and 0.38% of the essential amino acid methionine[17, 18].

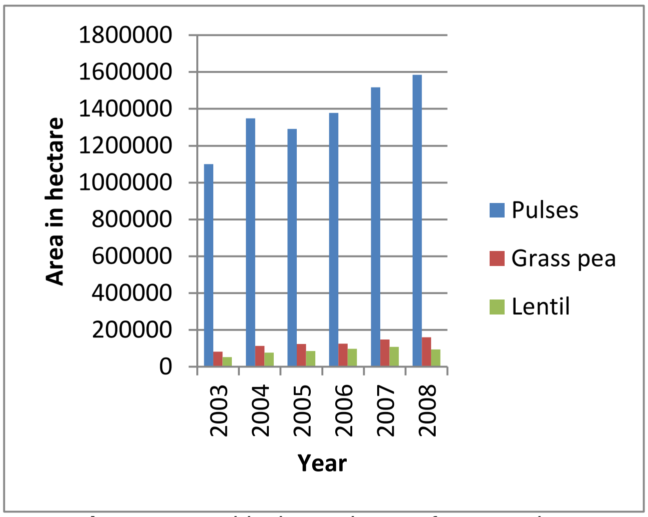

Figure 1. *In Ethiopia, total area of acreage in farming pulses has been increasing during the past decade; the rise in grass pea farming has surpassed lentil farming.*

Prolonged consumption of diets deficient in methionine and cysteine can deplete the body of glutathione, which is one of the body's chief metabolic defense system against oxidative stress. Hence, developing varieties with higher methionine and cysteine contents may be more relevant in improving the nutrition without losing the hardy nature of grass pea. Defining a cut-off threshold level of safe ODAP content has not been achieved at a scientific consensus[10]. By virtue of being a flowering and hanging plant, seed content of ODAP is highly influenced by cross-pollination activities of bees[10]. Higher ODAP level confers higher resistance to biotic and abiotic stresses to the plant[10].

Although epidemics of neurolathyrism have not happened in Ethiopia within the past decade or so, there is a potential that farming community can switch to a monotonous grass pea diet when other types of staple crops become challenging to have a continuous supply due to crop market globalization and global weather fluctuations. Underutilized and neglected crops such as the grass pea may receive more attention when countries face challenges in reaching to the rising demand of staple crop supply. Current research emphasis should not be on lowering the ODAP content; rather, it should be on boosting seed contents of sulphur-containing essential amino acids like methionine and cysteine in grass pea genotypes. A paradigm shift in grass pea genetic improvement is underway, and these genes are getting the attention of different stakeholders of research laboratories in Ethiopia. While the ultimate goal towards control of neurolathyrism is achieved by poverty reduction at communal level, efforts to address questions surrounding risks in grass pea feeding need to be adequately addressed. Countries in Europe are rediscovering and reintroducing lathyrus seeds into their farming practices for consumption[10, 19].

***Guaya*: local experience, and views**

The labeling of 'famine-food' is a misnomer since the grass pea is also heavily consumed during times of heavy rains and monsoon due to its inherent capacity to resist both ends of weather calamities. Its mere availability during both dry and rainy seasons makes local community to practice a monotonous consumption which when combined with deficiency of sulfur-containing amino acids can ultimately result in the development of neurolathyrism. In Ethiopia, many affected people continue consumption despite their awareness of its possible toxicity; this reminds that people's perceptions about disease causation is important in the context of managing diseases in patients' own perception, experience, cosmovision, traditional practices, biopsychosciospiritual model of health and disease. Some local and folkloric explanations provide that it is overconsumption of the freshly harvested seeds which lead to crippling, while other observations claim there is also inhalational component of the toxin being inhaled overnight - based on the fact that young male farmers consume and pass the night in their farm barns where they store harvested crops following a typical day of exhaustion at the farmlands.

International scientific interest needs to build up so as to reassure progress on methodological studies regarding neurolathyrism.

Neurolathyrism needs to be classified as a reportable disease, since it occurs in epidemics resulting in irreverisible spastic myelopathy afflicting younger age-group demographics who are at their peak productive years – hence, with accrued wider socioeconomic consequences. Adulteration techniques during food processing not only reduce the concentration of neurotoxin, but also can provide protective nutrients such as methionine, homoarginine, other anti-oxidants, and vitamins[5]. As discussed above, the ODAP toxin is more damaging in the face of inadequate supplementation of sulfur-containing amino acids, other antioxidants, and in general a balanced diet. It is not uncommon to observe a young male with scissoring gait walking with cane support on the streets and thoroughfares of metropolitan Addis Ababa and nearby cities. Victims migrate to the cities searching for job opportunities, exposing the high socioeconomic burden and family destabilization. The commonly afflicted victims are young males of a remotely located rural farming family; these young males are the bread winners of their family, on whom their family members heavily rely on. It is not hard to imagine the burden linked to this disease, as these young males suddenly give up their farming practices owing to their irreversible disability; this leads to crop failures, high economic loss, and associated psychosocial consequences. Neurolathyrism is not merely a medical disability with lifelong suffering, but also results in a wider affliction ranging from unplanned emigration, family separation, socioeconomic loss, and continued search for chronic support system.

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Yohannes W. Woldeamanuel

Department of Neurology and Neurological Sciences, Stanford University School of Medicine, Room H3160, 300 Pasteur Drive, Stanford, CA 94305-5235, USA. Email: yohannes.woldeamanuel@gmail.com; ywoldeam@stanford.edu

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Grasspea: A crop for the poor

In India, Grasspea, locally known as *Khesari / Lakh / Lakhadi* or *Teora* is a winter pulse crop. Being a minor crop its exact production statistics does not appear at national level. When other crops fail due to adverse conditions, grasspea becomes the only available source of food for the poorest sections, and sometimes it is the food for survival in times of drought-induced famine. It is predominantly grown as a relay crop in rice fields, which is an established popular rice-based cropping system, and farmers do not have a better alternative under such harsh rain fed conditions. Because of its easy and low-cost cultivation, and resistance to drought, excess moisture, salinity, diseases and insect pests, farmers are attracted to grow this crop. It is a rich source of protein (up to 34%) and contains essential micronutrients, thus provides nutritional security to its consumers, particularly to the low income people in the society.

Farmer in grasspea field at Murshidabad (WB)

Despite all these merits, grasspea has an ambivalent reputation. Its seed contains a toxin, Beta-ODAP (β-N-oxalyl-L-α,β-diaminopropionic acid), which causes neuro-lathyrism a “nutritional curse” if consumed in excessive quantities for a long period of 4 to 5 months continuously. Grasspea is largely being used as adulterant with other pulses; therefore cultivation of low-ODAP or ODAP-free cultivars is highly desirable. In this endeavour, low-toxin (<0.1%) grasspea varieties with higher yield having desirable attributes like disease and pest resistance along with matching production technologies have been developed by various Indian institutions and ICARDA.

Women’s training for removal of toxin from grasspea

Under National Food Security Mission (NFSM)-Pulses, Govt. of India, ICARDA is providing these low ODAP cultivars like Ratan (0.06%), Prateek (0.08%), Mahateora (0.07%) and Nirmal (0.15%) to the farmers to make them aware about the new improved low toxin and high biomass varieties. ICARDA has worked in Chhattisgarh, Uttar Pradesh, Bihar and West Bengal states of India with Indian partners. Through the baseline survey it was observed that most of the farmers were not aware about the low toxin and high biomass improved varieties of grasspea, they were also not aware about the soil testing to apply fertilizers to the crop, no knowledge of post-harvest technologies related to the crop etc. A total of 123 villages have been covered by ICARDA and its national partners with the involvement of 1959 farmers directly and 636 ha area have been replaced with the low toxin and high biomass improved varieties.

Chopping of green grasspea for fodder

Demonstrations were conducted by different collaborating centers at the farmers’ fields with low-ODAP high yielding grasspea varieties, *viz.* Nirmal, Ratan, Prateek and Mahateora for demonstrating advantages of the new improved, low-ODAP, high yielding varieties and improved cultivation practices over the traditional way of cultivation with high ODAP materials. The variety Nirmal gave 26% higher yield over the traditionally grown grasspea varieties/landraces by the farmers. The farmers selected the two best varieties, *viz.* Ratan and Nirmal from eastern India and Ratan and Mahateora from central India. Trials were conducted to assess the impact of improved *vs.* local varieties and improved technology *vs.* farmer practice which revealed yield advantage of up to 46.96 and 84.75%, respectively. The project was implemented in the traditionally grasspea growing area, rice-fallows and degraded lands without replacement of any other crop. With the enthusiasm and interest of farmers a total of 4176 q of the quality seed have been produced by the farmers during three years.

To make farmers aware about the improved varieties and production technologies, different extension activities like Farmers’ Training, Field Day, Awareness Camps and Travelling Seminar etc. have been organized by ICARDA and its national partners at different locations. These extension activities were attended by participating farmers and non-participating farmers. More than 3500 farmers were trained under this program which includes more than 600 women who attended training programs. Women farmers were trained in physical detoxification of the grasspea seeds. Four seed hubs have been created by the famers association for timely availability of the improved seed and seed security. Different extension materials like leaflets, booklets, folder etc. in different regional languages have been distributed to the farmers. Through ICARDA's initiative farmers are now aware about the low toxin & high biomass varieties and they are very much interested to grow and adopt these varieties. Farmers are very happy and enthusiastic about the expansion in the area under grasspea cultivation. They are also disseminating/exchanging these improved varieties to the neighbouring farmers and villages to replace the old and traditional varieties of the grasspea. Grasspea is a crop which requires less care and inputs and gives feed, fodder and nutritional security to the poor farmers in addition to other indirect benefits like nitrogen fixation etc. Proper attention should be given to this multi-purpose crop.

[1]

Ashutosh Sarker, PhD.
Regional Coordinator & Food Legume Breeder
ICARDA South Asia & China Regional Program
2nd Floor, Office Block-C, NASC Complex,
DPS Marg, New Delhi-110012, India
Web: www.icarda.org

A lady preparing and selling grasspea *Pakora* in a village market

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