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Consumption of pesticide-treated wheat seed by a rural population in Malawi

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Abstract

An outbreak of typhoid fever in rural Malawi triggered an investigation by the Malawi Ministry of Health and the Centers for Disease Control and Prevention in July 2009. During the investigation, villagers were directly consuming washed, donated, pesticide-treated wheat seed meant for planting. The objective of this study was to evaluate the potential for pesticide exposure and health risk in the outbreak community. A sample of unwashed (1430 g) and washed (759 g) wheat seed donated for planting, but which would have been directly consumed, was tested for 365 pesticides. Results were compared with each other (percentage change), the US Environmental Protection Agency's (EPA) health guidance values and estimated daily exposures were compared with their Reference dose (RfD). Unwashed and washed seed samples contained, respectively: carboxin, 244 and 57 p.p.m.; pirimiphos methyl, 8.18 and 8.56 p.p.m.; total permethrin, 3.62 and 3.27 p.p.m.; and carbaryl, 0.057 and 0.025 p.p.m.. Percentage change calculations (unwashed to washed) were as follows: carboxin, -76.6%; pirimiphos methyl, +4.6%; total permethrin, -9.7%; and carbaryl

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CONFLICT OF INTEREST

The authors declare no conflict of interest.

Disclaimer

The findings and conclusions in this article are those of the author(s) and do not necessarily represent the views of the Centers for Disease Control and Prevention or Agency for Toxic Substances and Disease Registry. The seed pictured in the photo is not the seed tested by FDA Laboratories.

–56.1%. Only carboxin and total permethrin concentration among washed seed samples exceeded US EPA health guidance values ($285 \times$ and seven times, respectively). Adult estimated exposure scenarios (1 kg seed) exceeded the RfD for carboxin ($8 \times$) and pirimiphos methyl ($12 \times$). Adult villagers weighing 70 kg would have to consume 0.123, 0.082, 1.06, and 280 kg of washed seed daily to exceed the RfD for carboxin, pirimiphos methyl, permethrins, and carbaryl, respectively. Carboxin, pirimiphos methyl, permethrins, and carbaryl were detected in both unwashed and washed samples of seed. Carboxin, total permethrin, and carbaryl concentration were partially reduced by washing. Health risks from chronic exposure to carboxin and pirimiphos methyl in these amounts are unclear. The extent of this practice among food insecure communities receiving relief seeds and resultant health impact needs further study.

Keywords

pesticide; seed; exposure; environment; carboxin

INTRODUCTION

In times of drought and food scarcity, remote, impoverished, and rural communities may turn to unusual or even dangerous foodstuffs to survive. During 2007, a fatal outbreak of illness occurred among villagers in Bangladesh when they consumed *Xanthium strumarium* seedlings (commonly known as cocklebur) after destructive monsoon flooding eliminated most of the available local food supply.¹ Consumption of large amounts of these seedlings resulted in nausea, vomiting, loss of consciousness, hepatotoxicity, and in some cases, death among villagers.¹ Epidemics of lathyrism and neurolathyrism, a condition resulting in irreversible spastic paraparesis (extremity weakness) of the lower limbs resulting from ingestion of the grasspea (*Lathyrus sativus*), have occurred throughout history in times of drought and food shortages.^{2,3} Konzo, a permanent spastic para- or tetraparesis, is reported to occur during dry seasons and is associated with consumption of improperly prepared cassava (*Manihot esculenta*).⁴

Seeds, wheat seed in particular, may be used to prepare foodstuffs such as homemade bread by certain populations even when food is not scarce. An outbreak of severe alkyl mercury poisoning occurred in Iraq during 1971–1972 when villagers prepared bread from seed treated with a mercurial fungicide. Previous similar outbreaks had occurred in 1956 and 1960 in Iraq.⁵ During the growing seasons of 1963–1965, an outbreak of methylmercury dicyandiamide poisoning occurred in Guatemala from wheat seed treated with this agent.⁶ Based on historical outbreaks, consumption of pesticide-treated seed or food products prepared directly from pesticide-treated seed can present an acute health risk.

During a recent international outbreak investigation, the local community was discovered to be chronically consuming wheat seed intended for planting. Staff from the Malawi Ministry of Health (MOH) and the Centers for Disease Control and Prevention jointly investigated an outbreak of neurological illness in a rural village that straddled the border of Malawi and Mozambique in 2009. The etiology of the outbreak was ultimately determined to be typhoid fever, a systemic illness caused by *Salmonella enterica* serovar Typhi. Similar neurological

signs have been previously reported as a complication of typhoid fever.⁷⁻⁹ During the outbreak investigation, the team discovered that villagers were consuming wheat seed provided by a non-governmental organization (NGO) as part of a program in which seed meant for planting is provided at little or no cost and a certain amount is later repaid after harvest. There had been a poor crop yield last season and there was a resultant food shortage, hence the community was directly consuming some of the seed. The seed had a pink-colored dusty coating that often indicates that a pesticide was applied. Community members would wash the seeds before eating them, believing that this removed the pesticides. To determine whether a public health threat existed from this practice, a sample of unwashed and washed wheat seed was collected from local villagers and shipped to a US Food and Drug Administration (FDA) laboratory for pesticide analysis.

The objectives of this investigation were as follows: (1) to determine which, if any, pesticides were present on both unwashed and washed seed samples, (2) determine whether rinsing in water affects pesticide concentration, and (3) determine whether pesticide concentrations, if present, represent a potential public health threat.

METHODS

Seed procurement

Approximately 1430 g of unwashed wheat seed, donated to the community for planting, was purchased from a local community member in the outbreak village. Approximately 759 g of the wheat seed donated for planting that had been washed in preparation for consumption was then purchased from a different resident and household (a neighbor) in the same village. Both samples were from the same original supply of wheat seed provided by a NGO to the community and both were designated for consumption by community members. The seeds were washed by rinsing them in a bag with water from a nearby stream and then allowing them to dry in the sun on a mat. This is the typical process used by the villagers before consumption (Figure 1). This yielded one sample of unwashed seed and one sample of washed seed for testing.

Laboratory analysis

All analyses were completed by the Northeast Regional Laboratory of the US FDA. The extraction method for the wheat seed was from the Pesticide Analytical Manual (PAM),¹⁰ section 302 E4, the recommended method for non-fatty, low-moisture commodities. The method involves extraction with water/acetone followed by liquid-liquid partitioning with petroleum ether/methylene chloride. Each sample was separately mixed by hand and half of the total amount was composited to powder by an electric blender. Then the resulting powder was mixed again by hand and 25 g from each the unwashed and washed composited samples was analyzed by the PAM method.¹⁰ The extract was cleaned according to the PAM,¹⁰ section 302 C6 with a SAX/PSA cartridge that allows both polar and non-polar residues to be recovered. The determination/detection step used Agilent 6890N/5973N gas chromatograph/mass selective detectors in selective ion monitoring mode for organohalogen, organonitrogen, and organophosphorus compounds, which currently detects ~350 analytes. The US FDA laboratory tested for 365 different pesticides, including various

different insecticides and fungicides, and reported results as p.p.m. or mg/kg, which are equivalent.

Comparison of washed seed results to unwashed seed results

Pesticide testing results were compared between unwashed and washed samples to determine whether the pesticide present was partially or completely removed by washing. Percentage change was calculated between the two results by subtracting the unwashed result from the washed result and dividing that number by the unwashed result and then multiplying by 100%.

Comparison with the US Environmental Protection Agency's (US EPA's) tolerance values

Pesticide residue amounts were compared with tolerance values for these agents on wheat. Tolerance values are set by the US EPA and represent the maximum amount of pesticide that can remain in foodstuffs marketed in the United States. In instances where no specific tolerance value for an agent in wheat existed, the tolerance value for that agent in aspirated fractions of grain (various different plant parts that are aspirated during normal handling of grains) was selected for comparison by the study authors.

Comparison of estimated daily exposures with the US Reference Dose (RfD)

The US EPA defines the RfD as an estimate of a daily oral exposure to the human population that is likely to be without an appreciable risk of adverse health effects over the course of a lifetime. RfDs are often based on longitudinal animal studies (e.g., rodents). The RfD includes uncertainty factors to reflect limitations in the data, uncertainty in applying animal data to humans, sensitive subpopulations, and can be greater than an order of magnitude.^{11,12} The RfD is expressed in milligrams of agent per kilogram of body weight per day (mg/kg/day). These values are listed in Table 1. To determine the estimated daily exposure of adults in Malawi consuming washed seeds, an estimate of the amount of seed eaten per person was needed. Representatives of the Malawi MOH with knowledge of local practices estimated that daily wheat seed consumption in adults was ~1 kg based on discussions with the community members who provided the seed. Washed wheat seed testing results are in p.p.m. or mg/kg of agent. Estimated daily exposures in 70 kg adults (the average weight of an adult) were calculated by taking the chemical concentration on washed seeds in mg/kg, multiplying by 1 kg/day and then dividing it by 70 kg to obtain a value in mg/kg/day. This value was then compared with the RfD, expressed in mg/kg/day also.

Minimum amount of washed wheat seed needed to reach the US EPA's RfD

The amount of pesticide needed to achieve the RfD for each agent (assuming 100% absorption) was estimated for a 70-kg person. This value was then divided by the amount of chemical found on the washed wheat seeds in p.p.m. or mg/kg to yield the amount of seed in kg/day that would need to be consumed to reach the RfD (in a 70-kg adult).

RESULTS

Of the 365 compounds tested, the following pesticides were detected and quantified: carboxin, pirimiphos methyl, permethrins, and carbaryl. Results are listed in Table 1. The remaining compounds were not detected.

Carboxin

Carboxin was detected in both the unwashed (244 p.p.m.) and washed (57 p.p.m.) seed samples. There was a 76.6% decrease in carboxin concentration after washing (although washing did not completely remove the agent), suggesting that washing substantially reduced pesticide concentration. Carboxin concentrations in both washed and unwashed wheat seed samples substantially exceeded the specific US EPA tolerance level (0.2 p.p.m.) for wheat.¹³ Testing results were 285 and 1220 times the US EPA tolerance level for the washed and unwashed samples, respectively. The estimated daily exposure for carboxin from washed wheat seed (57 p.p.m.) in a 70-kg adult villager was approximately eight times higher than the RfD for this agent. The amount of washed wheat seed needed to exceed the RfD for these agents is 0.123 kg, an amount easily exceeded based on the estimated amount of seed consumed by adults (estimated as 1 kg).

Pirimiphos methyl

Pirimiphos methyl was detected in both unwashed (8.18 p.p.m.) and washed (8.56 p.p.m.) seed samples. There appeared to be a 4.6% increase in pirimiphos methyl concentration between unwashed and washed seed samples, suggesting that washing had no effect. There is no specific US EPA tolerance value for pirimiphos methyl in wheat. Therefore, we used an alternative guidance value. A comparison level of 20 p.p.m. was used, which was taken from the guidance value for pirimiphos methyl in aspirated fractions of cereal grains (grain dust) group as per CFR180.409.¹³ Testing results for pirimiphos methyl did not exceed this value, although it slightly exceeded the tolerance value for itself in two other grains (corn and sorghum, 8 p.p.m.).¹³ The estimated daily exposure for pirimiphos methyl in a 70-kg adult villager was ~12 times higher than the RfD for pirimiphos methyl. The amount of washed wheat seed needed to exceed the RfD for pirimiphos methyl is 0.082 kg. Adults consuming the daily estimated amount of washed wheat seed (1 kg) would be expected to easily exceed the RfD for pirimiphos methyl.

Total permethrins

Permethrins were detected in both unwashed (3.62 p.p.m.) and washed (3.27 p.p.m.) wheat seed samples. Washing appeared to reduce the total permethrin concentration by 9.7%. There is no specific US EPA tolerance value for all permethrins in wheat; however, results also exceeded the next most appropriate comparison value of 0.5 p.p.m. for aspirated fractions of cereal grains group as per CFR180.378.¹³ Testing results were approximately seven times higher than the US EPA tolerance level for both samples. The estimated daily exposure in an adult for permethrins was slightly less than the maximum acceptable daily dose based on the RfD in a 70-kg adult for this agent. Adults would have to consume only slightly (> 1.07 kg) the estimated 1 kg of seed reported by the community to exceed the RfD for this agent.

Carbaryl

Carbaryl was detected in both unwashed (0.057 p.p.m.) and washed (0.025 p.p.m.) wheat seed samples. Washing appeared to reduce carbaryl concentration by 56.1%. Both values were well under the US EPA tolerance level for carbaryl in wheat (1 p.p.m.).¹³ The estimated daily exposure of carbaryl in a 70-kg person was ~278 times less than the daily dose in a 70-kg adult based on the RfD. Adults would have to eat ~280 kg of washed wheat seed during any given day to exceed the RfD for carbaryl.

DISCUSSION

Carboxin, pirimiphos methyl, permethrins, and carbaryl were found on both washed and unwashed samples of wheat seed intended for planting but being consumed directly by a community straddling the border of Malawi and Mozambique. Carboxin in particular had substantially elevated concentrations in both washed and unwashed seed samples. Washing did not remove all pesticides: consumption of washed seed samples may still expose the consumer to potentially harmful pesticides.

When compared with the other agents, carboxin had the highest concentrations on both washed and unwashed seed samples. Very little is known about the metabolism, biotransformation, and toxicity of this compound in humans. No reports of acute or chronic oral dosing studies or outbreaks of illness in humans were identified in the literature. One case report of a 7-year-old boy who ate several handfuls of carboxin-treated wheat seed was identified. This patient developed vomiting and headache within the first hour of ingestion, but symptoms rapidly improved after administration of an emetic.¹⁴ It is unknown if the patient's symptoms were due to carboxin, another agent, or the seeds themselves (e.g., mechanical irritation). Rodent studies have identified liver and kidney changes as a result of chronic exposure to carboxin.¹⁵ No acute dietary risk assessments were performed, and chronic risks from food in the United States were determined to be below the US EPA's level of concern; therefore, little data are available on this topic.¹⁵ At this time, there is insufficient information to determine whether a chronic health threat exists from exposure to foodstuffs with these amounts of carboxin.

Pirimiphos methyl is an organic phosphorous compound (OPC). OPCs are used as insecticides and irreversibly inhibit the enzyme acetylcholinesterase, which breaks down acetylcholine at neuronal synapses and the neuromuscular junction.¹⁶ OPC acutely poisoned patients may develop signs and symptoms of a peripheral neuropathy after poisoning (evidence of peripheral neuropathy was not consistently observed in the patients examined in this outbreak). Some occupational exposure studies (typically with inhalational and/or dermal exposures of OPCs) have also found associations between chronic OPC exposure and electroencephalographic abnormalities, sensory and motor peripheral neuropathies, neuromuscular dysfunction, neuropsychiatric and behavioral disturbances, parkinsonism, contact dermatitis, and even asthma.^{16–20} Although testing results on both washed and unwashed seed samples did not exceed the tolerance value in aspirated fractions of grain used for comparison, they did slightly exceed the tolerance values for it two other grains (corn and sorghum). In addition, estimated daily exposures to this agent from consumed wheat seed did exceed the RfD. They did not, however, exceed the experimental dose listed

by the EPA as the no observed effect level or NOEL (as demonstrated by transient plasma cholinesterase activity depression), measured as 0.25 mg/kg/day in animal studies.²¹ Therefore, acute toxicity at these exposure amounts is probably unlikely. Exposure to this agent in these doses probably does not pose an acute public health threat; however, the risks associated with chronic exposure to this agent in these amounts, including the development of peripheral neuropathy, are unclear.

Permethrins belong to a class of insecticides known as the type 1 pyrethroids. Pyrethroids are synthetic derivatives of naturally occurring substances with insecticidal activity found from extracts of the flower *Chrysanthemum cinerariaefolium*. They have little mammalian toxicity because of their rapid metabolism and do not persist for long in the environment. In animals, large, acute doses of type 1 pyrethroid toxicity can cause extensive tremors, twitching, increased metabolic rate, and hyperthermia (fever). However, in general, the type 1 pyrethroids are unlikely to cause systemic toxicity in humans unless large amounts are ingested (e.g., suicide attempt).²² No reports of chronic oral dosing studies with permethrin in humans were identified in the literature from which to compare findings from this outbreak. Although testing results for permethrins were above existing tolerance values, and the estimated daily exposure was similar to the RfD, the NOEL for this agent (based on animal data) is much higher (5 mg/kg/day).²³ Based on what is known about permethrins, the estimated exposure amounts from this study, and the fact that any actual dose (implies absorption) is less than the estimated exposure, we feel that permethrins (in this situation), most likely do not pose a significant acute or chronic public health threat.

Carbaryl is a carbamate insecticide that inhibits acetylcholinesterase, the enzyme responsible for metabolizing the neurotransmitter acetylcholine after normal neuronal depolarization. It does this reversibly, in contrast to the similar acting OPCs, which, over time, will bind irreversibly. Peripheral neuropathy may occur due to chronic oral administration of carbamates.²⁴ However, chronic human ingestional exposures to carbamates and their associated toxicity patterns are incompletely described and defined. One human study that orally dosed volunteers with carbaryl at 0.06–0.13 mg/kg daily for 6 weeks found no deleterious changes. In this case, the maximum daily dose for a 70-kg adult would have been 9.1 mg; the estimated daily exposure amount in this study was 3.27 mg.²⁵ Long-term follow-up of acutely or chronically carbamate exposed individuals in general has been incomplete, but a variety of neurobehavioral effects have been reported such as fatigue, lethargy, mood changes, poor coordination, and others.^{26,27} Chronic carbamate exposure in these doses would not be expected to pose a significant acute or chronic health threat based on currently available data.

Anecdotal reports from Uganda and other countries suggest that the practice of eating seed donated or otherwise provided from NGOs for planting may be widespread in Africa and other parts of the world, especially during periods of food insecurity. However, there is an absence of data characterizing the extent of this practice and associated health risks from long-term exposure. Washing appeared to reduce the amount of three pesticides (carboxin, permethrins, and carbaryl) in our study but did not remove all of any of the pesticides. Of particular note was that washing did not appear to reduce the concentration of carboxin to an amount considered even close to an exposure without any health risk (below the RfD) in our

estimated exposure scenarios. These limited results suggest that washing alone is not effective in removing all risk of pesticide exposure, but may reduce the risk of exposure for some pesticides. The reason for the small increase (4.6%) in pirimiphos methyl concentration in the washed seed sample when compared with the unwashed sample is unclear, but may be because of normal measurement variability associated with testing concentrations in such small amounts. Although this was a very limited study (two samples), it does raise concern, that this practice may be associated with the potential for a public health threat from certain pesticides such as carbaryl and primiphos methyl, especially in the chronic exposure setting. The extent and severity of any such threat is dependent on type and concentration of pesticide used, washing practices, duration, and type (consistent, intermittent, etc...) of exposure.

Several suggestions were communicated to the Malawi MOH for consideration. They included consideration toward enacting a public health information campaign to advise villagers that washing does not remove pesticides from the seeds and advising villagers to discontinue the practice of eating either washed or unwashed seeds intended primarily for planting due to unknown health risks. Finally, there is a known health risk associated with exposure to OPCs. In the estimated exposure scenarios discussed previously, there is potential to easily exceed the pirimiphos methyl RfD guidance value. Implementation of surveillance for syndromes consistent with cholinergic poisoning should be considered.

There is very little information on clinical effects resulting from chronic ingestion of these agents. The amounts ingested as outlined in Table 1 are estimated exposure amounts and not true doses. These agents would have to be absorbed into the body after ingestion, and each has a different bioavailability value. Therefore, the actual dose from the exposure would likely be less than what has been estimated. It is important to note that in the United States, if no tolerance value exists for a chemical for wheat, then any amount of agent present would not be tolerated and the foodstuff would be removed from the market. However, this practice may not apply to all countries; final decisions regarding acceptability or tolerance values are up to the appropriate national or local public health authority.

Limitations

Our results and exposure scenarios were reliant on a single sample of washed and unwashed seed from different sources. The original pesticide concentrations in each sample may have differed before washing. Washing techniques could also vary from person to person that could account for differences. We also were unable to systematically collect data on washing techniques and dietary patterns from a representative sample of the community. Considerable variability in pesticide concentration, along with washing efficacy, may exist between lots of the same seed. Specific EPA tolerance values for two of these agents (pirimiphos methyl and permethrins) were not available for wheat seed, and a less specific alternative tolerance value was used for comparison. For carbaryl, it was noticed that the wheat-specific tolerance value was much lower (1 p.p.m.) than the value for aspirated fractions of grains (70 p.p.m.). Therefore, using non-specific tolerance values for comparison is not ideal. If the agent-specific tolerance value is indeed lower than the value in aspirated grain fractions then health officials may be falsely reassured that chemical

residue testing results are below maximum acceptable concentrations (such as with our pirimiphos methyl results) or are perceived to be less elevated than if compared with a known agent-specific value (e.g., permethrins). Interpretation of testing results, especially for agents without agent-specific tolerance values, should be cautious and include multiple scenarios (such as dose or exposure estimation, comparison with other established guidelines, etc...). Finally, these findings can not necessarily be applied to different grains and seeds in this, or other, populations.

CONCLUSIONS

Populations directly consuming seed meant for planting are likely at risk for unintended exposure to pesticides. Washing may reduce, but not completely eliminate, the concentration of some, but not all pesticides. Adverse effects on health will be dependent on factors such as type and amount of pesticide used, amount of seed consumed and domestic food handling practices. The risk of long-term effects from chronic exposure to pesticides such as carboxin and pirimiphos methyl in the amounts described is unclear and of some concern, while the risk of significant long-term effects from chronic exposure to permethrin and carbaryl in these amounts is probably small.

NGOs and relief agencies need to be aware that donated or otherwise provided (e.g., seed provided at little or no cost as part of subsidization program) may be directly consumed, which not only undermines the intent of providing seeds to improve long-term food production but could also adversely impact health. Consumption of pesticide-treated seeds may further undermine the health of already challenged populations, facing the larger health threat of food insecurity. The extent and potential public health impact from this practice is unknown and needs further study to ensure that this food safety issue is not adding to existing food security threats.

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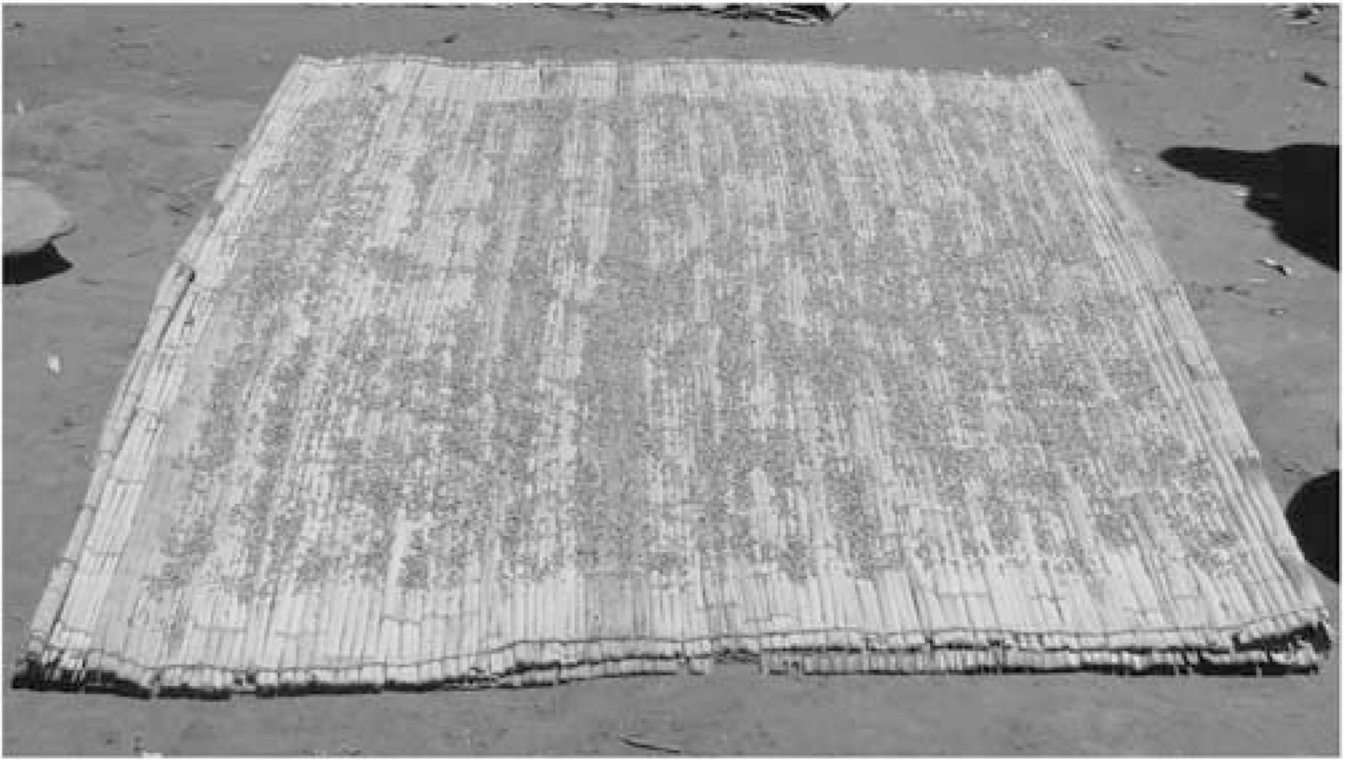


Figure 1.
An example of how wheat seed is dried and before consumption after being washed in water from a nearby stream.

Testing results, US EPA tolerance values, reference dose, estimated daily exposure calculations, and estimated seed consumption values needed to exceed the RfD for each pesticide.

Table 1

Pesticide	Amount on unwashed wheat seeds (p.p.m.)	Amount on washed wheat seeds (p.p.m.)	Percent change (± %)	US EPA tolerance values (p.p.m.)	RfD (mg/kg/day)	Estimated daily exposure (mg/kg/day)	Washed seed necessary to be eaten to exceed the US RfD in a 70 kg adult (kg/day)
Carboxin	244	57.0	-76.6	0.2 ^a	0.1	0.81	0.123
Pririmphos methyl	8.18	8.56	+ 4.6	20.0 ^b	0.01	0.12	0.082
Total permethrins	3.62	3.27	-9.7	0.50 ^c	0.05	0.047	1.07
Carbaryl	0.057	0.025	-56.1	1.0 ^d	0.1	0.00036	280

Abbreviations: EPA, Environmental Protection Agency; RfD, reference dose.

Discussions with the community revealed that adults may be eating as much as 1 kg of washed seeds daily.

^aFor wheat (from treatment of seed before planting) as per CFR180.378 (<http://www.gpoaccess.gov/cfr/>).

^bFor aspirated fractions of cereal grains group as per CFR180.409. (<http://www.gpoaccess.gov/cfr/>). No specific value for wheat available — the EPA tolerance value listed was the next most appropriate comparison value provided by the US Food and Drug Administration.

^cFor aspirated fractions of cereal grains group as per CFR180.378. (<http://www.gpoaccess.gov/cfr/>). No specific value for wheat available — the EPA tolerance value listed was the next most appropriate comparison value provided by the US Food and Drug Administration.

^dValue 1 p.p.m. for wheat as per CFR180.169. (<http://www.gpoaccess.gov/cfr/>).