J Food Sci Technol (May 2023) 60(5):1472–1482
https://doi.org/10.1007/s13197-022-05388-2

REVIEW ARTICLE

Regulatory landscape of risk assessment of pesticide residues in processed foods in India: a perspective

M. Muralidhara[1] · S. Mithyantha[2] · T. P. Rajendran[3] · Kaushik Banerjee[4]

Revised: 3 January 2022 / Accepted: 27 January 2022 / Published online: 16 February 2022

Abstract In India, the levels of pesticide residues in Raw Agricultural Commodities (RAC) are being subjected to adequate legal regulations, and the health-risks associated with them are determined from time to time adhering to global standards. Since RACs are generally consumed by humans as the processed foods (PF), it is imperative to monitor the levels of pesticide residues in them in order to approach a realistic analysis of dietary exposure and concomitant health risk assessment. In India, production and consumption of PFs have a rising trend and hence it is indispensable to monitor the residue levels of pesticides in largely consumed PFs. Depending on the processing methods and physicochemical properties of pesticides, the residue levels may decrease or increase in a PF when compared to the corresponding RAC. While obtaining data on processing factors (Pf), it is pragmatic to focus on those situations in which the residues get concentrated following the processing step. Currently, regulatory agencies of several countries and the CODEX have determined the levels of pesticide residues in processed agriculture commodities, arrived at the Pfs, and fixed the maximum residue levels. Since consumption of PFs in India has tremendously increased in recent times and there is paucity of data about their health risks/benefits, it is imminent to deliberate on the complexities associated with the issues of adopting the Pfs generated by other regulatory agencies and subsequently examine the possibilities of generating the required data on Pfs on a priority basis to enable a comprehensive risk assessment.

Keywords Pesticide residues · Raw agricultural commodity · MRL · Processing operations · Processed foods · Processing factor · Risk assessment

✉ Kaushik Banerjee
kbgrape@yahoo.com

[1] CSIR-Central Food Technological Research Institute, Mysore, B-24, Mallige road, J block, Kuvempunagar, Mysore 570023, India

[2] R&D, Rallis Research Centre, Bangalore, India

[3] India Habitat Centre, Research Information System for Developing Countries, RIS Block IV, Lodhi Road, New Delhi 110003, India

[4] National Reference Laboratory, ICAR-National Research Centre for Grapes, Pune 412307, India

Introduction

In India, the pesticide residue levels in raw agricultural commodities (RAC) are being subjected to adequate legislative and regulatory risk assessment studies from time to time adhering to the global food safety standards (Ambrus and Yang 2016; Bajwa and Sandhu 2014). In general, MRLs of pesticides are fixed on RACs. This is despite the fact that the agricultural commodities in most cases are not eaten raw, but are subjected to various processing methods prior to human consumption. Foods that are subjected to technological modifications either for preservation or for converting into ready-to-use foods are designated as "processed foods". Processing of an RAC may have significant impact on the pesticide residue levels in the final product. The residue levels may decrease, remain the same or increase in the processed fractions depending on the physico-chemical properties of the pesticide and its concentration in the RAC.

In India, food processing (FP) is one of the largest sectors in terms of production, growth, consumption and export. Trading of considerable processed foods in the international market entails generation of MRLs for processed commodities so as to evaluate their dietary risk assessment (India Food Report January 2018). To appreciate the need and relevance of fixing the MRLs of pesticides for the processed foods, one needs to examine the growth and current status of the FP industries.

Cursory glance of the FP industries in India

The food processing industries provide a vital linkage between industry and agriculture and are of enormous significance for India's economic development. Agrarian India has progressed from a position of scarcity to surplus in terms of production, and consequently, the opportunities for processing/production of processed foods has increased (India Food Report January 2018). Currently, the FP sector is recognized for its high growth rate/profits, thus, enhancing its contribution and significance to the world food trade. India is processing less than 10% of its agricultural output (~ 2% of fruits/vegetables, 6% of poultry, 21% of meat, 23% of marine and 35% of milk).

India is witnessing a major shift in consumption pattern towards the convenience food items, as evidenced by the fact that besides oils and fats, the convenience food items, ready meals, rice pasta/noodles and savory snacks have been registering impressive manufacture and market growth (Bren d'Amoura et al. 2020; Pandey et al. 2020). With the emergence of e-commerce, the food retail segment is further evolving. At the community level, a major shift in terms of altered consumption patterns due to urbanization, changes in the gender composition of the workforce, and the growing consumption rates of PFs are increasingly evident, which are largely driving the Indian market (Seto and Ramankutty 2016; Law et al. 2019).

Government of India has considered the FP sector a high priority industry and is promoting it with various fiscal reliefs and incentives. India's food processing sector is one of the largest in the world and its output is expected to reach $ 535 Billion by 2025–26. According to the Economic Survey 2021, the food processing industries have been growing at an average annual growth rate of around 9.99% over the five financial years that ended in 2018–19. Compared to agriculture (growing at 3.12%) and manufacturing (growing at 8.25%) sectors over the same period based on the 2011–12 prices, the FP sector embodies a significant segment of the Indian economy in terms of its contribution to GDP (Gross Domestic Product), employment and investment [Ministry of Finance (2021) Economic Survey Report].

Most of the processing practices in India can be classified into primary and secondary processing. While primary processing correspond to rice, sugar, edible oil, grain flour, seeds, bark, leaf and spices, the secondary processing includes the processing of fruits/vegetables (for beverages, sauces and ketchup, puree, etc.), dairy food products, bakery, chocolates and similar items. Primary processing offers a relatively lower value-addition compared to the secondary processing, and includes the processing of high-value items viz., beverages, sauces and ketchup, puree from fruits/vegetables, dairy food products, bakery, chocolates, etc.

In view of the tremendous growth of processed foods in the Indian market, it is highly imperative to assess the safety of these commodities to consumers by fixing the MRLs of pesticides and examining the plausible impact of residues pertaining to varied processing methods which are operational in both small-scale and large industrial settings. Only this would enable the stakeholders to self-assess the degree of compliance of the processed food products for global practices/legislation and meet the expected challenges in reaching the harmonization of food safety and global trade.

Processing factor (Pf) and their relevance

RACs are subjected to physical, chemical or biological processes to obtain the processed foods. Some common examples include milled grains, fruit juices and edible oils. Globally, various steps in simple culinary processes such as washing, trimming, peeling, cooking, baking etc. are considered to refine the dietary intake estimates. It is well documented that in majority of such cases, processing leads to a reduction in the load of pesticide residues attributable to either physical removal of residues or dissipation/degradation of residues during the processing steps (Holland et al. 1994; Keikotlhaile et al. 2010; Bajwa and Sandhu 2014; Kaushik et al. 2019). However, in certain specific situations there is a built-up (or enhancement) of residues, e.g., oil extraction from oilseeds, where the residues get accumulated in the oil fraction. In view of this it becomes a prerequisite that the processed foods are evaluated carefully for dietary health risk assessment. It is practically not possible to establish the MRLs for all the processed commodities due to their large variety and numbers. Hence it is suggested that the MRLs be fixed for those food items which receive significant exposure to pesticides at the pre-harvest level and where the residue is likely to get concentrated in the final product (Scholz et al. 2017).

In order to recognize and arrive at the processing factor/s, one needs to conduct well-designed processing studies. Processing of an RAC can lead to either an increase or a decrease in residues, depending on the specific processing method/s and more importantly the physicochemical properties of an active substance, especially its solubility characteristics. In several situations, the residues might remain the same on processing, indicating the complete mass transfer of the residues from the RAC to the PF. The effect of processing on residue levels in a processed product is the ratio of the pesticide residue concentration (mg/kg) in the PF to the concentration (mg/kg) in the RAC and designated as the Processing factor (Pf).

$$Pf = \text{level of residues in PF (mg/kg)}/\text{level of residues in RAC (mg/kg)}$$

A Pf greater than 1 indicates enrichment in the residue, while a reduction in the residue concentration in the processed product is expressed in a factor of less than 1. Under situations when the residues in an RAC get significantly reduced on processing, the MRL for RAC is directly applied to the PF (BfR 2016. http://www.bfr.bund.de).

Globally, the food safety regulatory agencies have recognized Pf as an indispensable tool, which is employed for providing data, (a) to the *regulatory bodies* on the extent/scope of changes in residue levels which occur during food processing, since these are critical to assess whether an RAC has been in compliance with the legal standards, (b) to *risk assessors* for refined dietary exposure estimates, which enables a realistic assessment in cases of the commodities that are consumed only after processing OECD Test Guideline (OECD 2008).

Processing operations—processed foods

Impact of processing on pesticide residues in food

The impact of processing operations of RAC on pesticide residues has been extensively studied and reviewed (Yigit and Velioglu 2020). These processes (domestic or industrial) generally involve transformation of a perishable RAC to a value-added product with enhanced shelf-life and nearly ready-to use form. While several processes result in a reduction of residue levels, a few may lead not only to enrichment in pesticide residues, but also may produce more toxic metabolites/ degradation products. Accordingly, understanding the impact of various food processing steps on pesticide residue levels has assumed significance in public health. A brief account of major processing methods is outlined below.

Washing Several evidences show that the washing process at home or in a commercial set up can significantly remove the surface-bound residue fractions through a physical process. The contact (non-systemic) pesticides are more prone to removal by washing compared to the systemic compounds. The fraction of residues that get absorbed and translocated to deeper tissue layers cannot be removed by washing.

Peeling This process significantly reduces the levels of pesticide residues in most fruits and vegetables. Although it removes the major fraction of non-systemic pesticide residues from the matrix, it is not effective in removing the residues of systemic pesticides since they get absorbed and translocated to deeper tissue layers.

Chopping Although chopping, cutting, crushing, mixing and other similar processes do not normally affect the pesticide residue levels directly, they may hasten specific reactions (e.g. hydrolysis, oxidation, etc.) and result in degradation of pesticide residues (Keikotlhaile et al. 2010).

Heat treatment With processing operations such as boiling, frying and pasteurization that involve heat treatment, reductions in pesticide residues might occur depending on the chemical nature of a pesticide. The degradation of pesticides on heat treatment mainly occurs due to oxidation and hydrolysis reactions, which mostly produce the metabolites or products of lesser toxicological significance (Kaushik et al. 2019).

Cooking Cooking, which involves heating, can cause degradation of pesticide residues and the extent is known to be affected by several factors e.g. cooking time, temperature, pH, etc. The residue levels after cooking might get modulated by a decrease in moisture content and also the nature of the cooking system.

Pasteurization/sterilization It is practiced extensively in the canning, milk and juice industries. The in-house experiments have indicated that sterilization is more effective in removal of pesticide residues compared to pasteurization.

Grinding of cereals Grinding of grains in hulls is shown to significantly remove pesticide residues.

Canning Several processing operations employed in canning industries (e.g. washing, peeling, blanching with water/steam or microwave for enzyme inactivation, pasteurization or sterilization) are shown to have a significant effect on the level of pesticide residues in the final product. For example, canning of tomatoes (heat treatment at 100 °C, 30 min) showed a greater reduction (71–86%) in residue levels of organophosphorus pesticides compared to the reductions (30–45%) of organochlorine pesticides (Yigit and Velioglu 2020).

Drying and powder grinding This process increases the concentration of pesticides proportionally in most cases, owing to the loss of water although residues may evaporate and/or degrade depending on the physico-chemical nature of the pesticide.

Fruit juice-concentrate production If fruit juice is produced without peeling, it is shown to contain higher levels of pesticide residues compared to the juices that are produced after peeling. The distribution of residues across the flesh and rind largely depends on the physico-chemical properties of the pesticide. Since the fat-soluble pesticides are removed to a large extent during centrifugation/ultra-filtration, only a small fraction of residues pass into the juice matrix.

Jam production Cooking under vacuum is widespread, and is usually applied for quite a long period with heating, which results in degradation of pesticides as well as their removal.

Malting, beer and wine production During malting/brewing, fermentation is the single-stage for pesticide residue reduction. In case of wine making, besides washing and fermentation, the maceration process also has a major effect on residue reduction.

Pickling While a large variety of vegetables/fruits are used for pickling, cucumbers are predominantly employed. Prepared either by natural fermentation or by direct addition of salt and vinegar, removal of pesticide residues is shown to be higher in non-fermentative process.

Dairy products Generally, pesticide residues are rarely detected in dairy products. Even though milk animals get exposed to pesticides while consuming any contaminated fodder/feed, during their metabolism, the ingested residues are reduced significantly or disappear depending on the amount and properties of the pesticide consumed. The semi-polar and polar compounds are less likely to get accumulated in milk. Since the non-polar pesticides of long persistence, e.g. chlorinated hydrocarbons and synthetic pyrethroids are largely discontinued in agriculture, the food safety non-compliance issues related to the dairy products are limited.

The behavior of pesticide residues in milk and milk products might be quite complex owing to the interactions with several matrix components of milk and a variety of processes involved in processing such as heating, fermentation, coagulation, fat separation etc. Hence, each of the dairy product/s should be studied individually to account for the influence of processing on the residue levels and derivation of Pfs.

Baking process This process employed for the preparation of bread, cakes, pastries, etc. involves prolonged cooking of food by dry heat, normally in an oven. Both duration of heating and temperature applied are considered as the critical parameters which can potentially influence the concentration of pesticides in the end products and the structure/texture of the products (e.g. biscuits) (Hakme et al. 2020).

Hot beverages Beverages such as tea and coffee are consumed in the form of water infusions of the prepared leaves or seeds as the case may be, and the most relevant part consumed is the perfusate or infusion. The RAC in the case of tea refers to the "made tea" i.e., processed, fermented and graded dry leaves. The MRLs for processed tea is calculated on the basis of pesticide residue in the infusion obtained by following a standard procedure for the preparation of the perfusate (Heshmati et al. 2021). For coffee, RAC refers to the dried coffee beans and the final consumed product is the infusion obtained from the fried and pulverized seeds. It must be noted that residues of relatively polar pesticides and/or their metabolites are generally higher in the infusion than the nonpolar or lipophilic compounds.

Alcoholic beverages-Malting and brewing These processes involve special treatments such as fermentation and distillation. The water-soluble components are more likely to get transferred to the beverages. Making of wine involves no dilution and hence the residue pattern will be different. Hence, depending on the initial residue levels in the RAC, the final processed beverage have to be carefully determined.

Irradiated foods Special considerations may be needed to study the influences on the residue dynamics while employing the irradiation process for preservation.

Oil production Generally, the pesticide level in an extracted oil sample depends on both the initial concentration (in RAC) and lipophilic/hydrophobic nature of the pesticide. Other processes (e.g. deodorization) employed during refining also have significant effects.

Post-harvest storage Under the stored conditions either in the cooler or deep freezer, pesticide residue levels are shown to remain stable or decrease very slowly. Temperature and the structure of the pesticide are shown to be critical during storage.

Processing operations likely to be of concern in terms of higher risk in processed foods

In general, some of the processes that are likely to pose higher risks owing to increased levels of pesticide residues have been largely recognized. The magnitude of such an increase is dependent on a host of factors viz., physico-chemical characteristics of a pesticide molecule, its major metabolites, thermal stability, lipophilicity, polarity and photo-stability (Scholz et al. 2017). Some of the major processing operations, which have been demonstrated to result in concentration of pesticide residues, are:

1. *(a) Cereal grain processing* Preparation of flour, bran and germs (particularly in wheat).
2. *(b) Fruit processing* Preparation of ketchup, paste, pomace and conversion to dry fruits (e.g., raisin, dry figs, etc.).
3. *(c) Oil extraction* Most pesticides with a high lipophilicity or octanol–water partition coefficient are known to get concentrated in the fat, and thus get extracted along with oil (as demonstrated with a

presence of higher residue levels in oil compared to the oilseed).

4. *(d) Drying Process* During conversion of raw red chillies to dry chillies, grapes to raisin making, egg and meat to the powder form etc. are known to result in higher concentrations of residues in the processed food matrices.

Pfs for processed foods: scenario in India

Currently, in India, there have been no systematic and comprehensive attempts to fix MRLs for processed foods (Kaushik et al. 2019; Bajwa et al. 2014). The exponential growth of processed food industries in the country entails the generation of Pf for at least a select number of PFs which will facilitate one to set meaningful MRLs of pesticide residues. It would be beyond the scope of this article to list all the processes involved with various PFs and the contribution to residue levels in the finished processed product, a data set is presented in Table 1 to illustrate the extent of residue levels in some processed foods. The residue levels presented pertain to the sum of the parent compound and the respective metabolites (as per the residue definition) (Codex Alimentarius 2016).

While data on the residues in Indian processed foods are scarce, in special situations of processing operations, a few processing factors (concentration factor) have been determined and MRLs established for only a small number of processed commodities such as drying of red chillies and oil-extraction.

Drying of chilli peppers In case of dried chilli peppers, as a special case, a generic processing factor is employed for the conversion of residues from fresh peppers to dried chilli peppers. Based on the available data, for the estimation of pesticide residue levels in dried chilli pepper a concentration factor of 10 has been recommended by Joint FAO/WHO Meeting on Pesticide Residues (JMPR) of Codex. Furthermore, the residue levels in dried chilli peppers should be determined based on the actual experimental data, and the relevant concentration factors should be applied to multiply the actual measured residue values in fresh chilli peppers and estimate the maximum residue and median residue levels from the converted data sets.

Oil extraction In this process, the concentration/dilution factors depend mainly on the type of processing and the extent to which the matrix of a meal and crude oil picks up a specific pesticide during crushing. The solubility of a pesticide in water or fat and in the solvents used in extraction is known to influence the levels of a pesticide in the processed product/s. In crude oils, MRLs can be determined based on the physico-chemical properties of the pesticide and the oil content of the RAC. Pesticides with high solubility in fat (or in the extraction solvents) are likely to get concentrated in crude oil. In such a situation, the MRL for crude oil will be the MRL for the oilseed (RAC) multiplied by a Pf.

Processed foods: issue of India-centric ethnic foods

India is witnessing a major shift in consumption pattern towards convenience food, which can be seen from the fact that apart from oils and fats, convenience food items, ready meals, rice, pasta & noodles and savory snacks have been registering impressive sales growth (Law et al. 2019). The cuisine in India is as vast and wide ranging as its multi-ethnic culture. The delicious and the exotic dishes of India are marked by the subtle uses of spices and herbs. Indian foods vary widely from region to region and hence require a focused approach to assess the possible associated risks. Furthermore, the issue of determining the residue levels in foods prepared from multiple components which are already processed is quite challenging since it involves a complex food matrix.

Determining the pesticide residues in complex food matrices

The issue of determining the pesticide residue levels in ready-to-eat foods is quite complex and needs special consideration. It is well known that extractability of pesticide residues is dependent on the biochemical nature of a food matrix. In general, the performance of a residue analysis method (recovery) is superior for predominantly water-rich matrices (e.g., grapes, tomatoes). On the other hand, the residue analysis in fatty matrices (e.g. nuts, oil seeds, etc.) often appears challenging, which is expressed in inconsistent or poor recoveries of most pesticides unless a proper cleanup step is executed.

Processing often changes the biochemical composition of a food matrix. In many cases, processing might enhance the complexity in matrix composition, and affect the method performance by lowering the accuracy and precision (repeatability and reproducibility). For example, when a fruit or vegetable consignment is dried, its moisture content is reduced significantly. The drying step also enhances the proportion of sugar and fatty components in the processed commodity, which adsorbs the pesticide molecules and affects their recoveries. Despite the fact that the drying step results in enhancements in residue concentrations, the extractability of pesticide residues in such matrices (e.g. raisins, mango leather, dried arils of pomegranate, etc.) is relatively poor in comparison to the fresh ones. The sample preparation procedure for residue analysis in such matrices thus usually requires inclusion of

Table 1 Residue levels of few pesticides in raw agriculture commodity and their corresponding residue levels in processed food and processing factor. *Source*: BfR (2016) http://www.bfr.bund.de. (accessed on 01.02.2021)

Compound	Raw agricultural commodity (RAC)		Processed food		Processing factor (Pf)
	Crop/produce	Residue level in the RAC (mg/kg)	Product	Residue level in the processed food (mg/kg)	
Captan	Grapes(fruit)	25	Dry fruit	50	2
Chlorpyrifos	Grapes	0.5	Dry fruit	0.1	0.2
Chlorpyrifos	Wheat grain	0.5	Wheat flour	0.1	0.2
Chlorpyrifos	Maize grain	0.05	Maize oil	0.2	4
Malathion	Wheat grain	8	Wheat flour	0.2	0.025
Malathion	Tomato fruit	3	Tomato juice	0.01	0.003
Malathion	Cotton seed	20	Cotton seed oil	13	0.7
Tebufenozide	Grapes(fruit)	2	Dry fruit	2	1
Clethodim	Cotton seed	0.5	Cotton seed oil	0.5	1
Clethodim	Soybean seed	10	Soybean oil	1	0.1
Clethodim	Rapeseed	0.5	Rapeseed oil	0.5	1
Kresoxim-Methyl	Olives	0.2	Olive oil	0.7	3.5
Cyhexatin	Apple (fruit)	0.09	Wet pomace	0.15	1.7
			Dry pomace	0.13	1.4
Deltamethrin	Black made Tea leaves	0.34	Tea brew	0.003	0.009
Bifenthrin	Black made Tea leaves	0.83	Tea brew	0.038	0.048
Hexaconazole	Black made tea	1.9	Tea brew	0.022	0.0114

additional steps for a better extraction efficiency of pesticide residues. For example, comminution of raisins usually requires pre-soaking in water for ~ 20–30 min and addition of water during blending to ensure appropriate homogenization.

Similarly, when oil seeds are processed to edible oils, the recoveries of pesticides might reduce significantly. This mainly happens because pesticides are mostly lipophilic in nature. A rise in fat content of a matrix reduces extractability of pesticides. Furthermore, whenever the fat content of a food matrix increases on processing, many of the matrix compounds, e.g. fatty acids, lipids, etc. get co-extracted along with the target pesticide residues. When such extracts are injected to a GC–MS or LC–MS instrument, the co-extracted compounds might cause enhancement or suppression in signal intensities of the target pesticides. This in turn results in over-estimation or under-estimation of pesticide residues. To overcome such problems, selective cleanup and applications of matrix-matched calibrations are required to be applied.

Application of processing factor/s (Pf)

Several key recommendations have been made while applying the Pfs derived from processing studies. Some of them are: (a) the best estimate of the processing factor should be applied for the estimation of MRL, HR-P (Highest Residue Level in a Processed Commodity) and STMR-P (Supervised Trials Median Residues) in processed commodities. (b) To estimate the MRL of a processed product, the MRL of the RAC is multiplied by the Pf derived from the residue definition for enforcement purposes. (c) For the purpose of IEDI (International Estimated Daily Intake) and IESTI (International Estimated Short-Term Intake) estimations, the STMR and HR of the RAC is multiplied by the Pf derived from the residue definition for dietary risk assessment (Pf RISK) to give the median and highest residue in the processed commodity.

Processing studies and their relevance

Objectives The main objectives of processing studies are (a) provide data on the metabolites/degradation products which need to be subjected to risk assessments separately,

(b) to ascertain the levels of residues in processed products that would help in the estimation of the Pf for the final products, and (c) provide reliable estimates of the chronic/acute dietary intake of pesticide residues.

The basic principles underlying the conduct of a processing study with an RAC which would be subjected to various processing methods have been described in the OECD guideline (OECD 2009). Further, specific data on a variety of processed commodities is published and illustrated with examples of types of processing operations (OECD 2008a; OECD 2008). Although a detailed description of these procedures is not in the scope of this article, striking features of the guidance document (Codex) have been briefly dealt below.

Essential aspects for conducting processing studies

Requirement Processing studies are highly essential when residue levels are significant in plants/plant products that are processed. If residues in an RAC are above 0.1 mg/kg, that is considered significant. For the fat-soluble pesticides, it is important to note that their residues might get concentrated in the oil fraction.

Selection of method The method opted should represent the likely uses of pesticides in agriculture for both domestic as well as industrial preparations of food and feed. However, industrial procedures may be preferred owing to the importance of industrial products in trade.

Basic design The design should allow to determine the Pfs and aid in recommendation of MRLs for processed foods/feeds which are important in trade. More than one study may be essential in order to generate consistent Pf data. The RAC employed for a processing study should be a field-treated commodity with quantifiable residues, so as to arrive at Pfs for the processed products. For this, field treatment at an exaggerated application rate may be necessary to obtain the residue levels at sufficiently high concentrations. Studies with spiked samples are generally not employed unless it is shown that the residue in the RAC is entirely located on the surface.

Optimum number of trials The robustness of the derived Pf is dependent on the number of replicate trials employed. As a standard practice, in a study, a third trial is necessary, when Pfs derived from two replicate trials show a variability above-50%.

RAC samples Under situations which require storage (frozen) prior to residue analysis, samples are to be drawn just before processing and also at the end of processing.

Validity of the analytical method The analytical methods viz., sample extraction and cleanup procedures should comply with the OECD Guidance Document (OECD 2009; OECD 2008b). Since in many cases, a processed product is largely different from its RAC in terms of biochemical composition, it is essential that a residue analysis method needs to be thoroughly standardized and validated in the processed matrix (as discussed under the section—Determining the levels of pesticide residues in complex food matrix).

A residue testing method needs to be optimized by standardizing the extraction and cleanup steps to improve accuracy and precision in analysis. The workflow of method validation involves a set of quality control parameters such as recovery rates, precision, reproducibility, etc., and the method performances should comply with the general principles laid down for analytical methods, for example, as in DG-SANTE of the European Commission (https://ec.europa.eu/food/sites/food/files/plant/docs/pesticides_mrl_guidelines_wrkdoc_2019-12682.pdf). The recoveries are considered satisfactory when those are in the range of 70–120% with the coefficients of variation below 20% ($n \geq 6$). Generally, a study is not accepted if these conditions are not fulfilled. As a routine requirement, spiked samples are to be run concurrently for quality control purposes. In case the residue definition includes metabolites, the dietary exposure assessment should consider the parent pesticide as well as the suggested metabolites. The use of certified reference materials, if available, is always beneficial from the point of view of acceptability to regulators.

Compliance to GLP (good laboratory practices) standards The processing studies that are conducted in accordance with the GLP standards are more accepted because the results of such studies ascertain uniformity, consistency, reliability, reproducibility, quality and integrity of safety tests. The GLP-based studies also provide all the background information related to the processing steps and their influence on the residue dynamics, and thus can systematically justify the derivation of Pf.

Calculation of processing factor (Pf) Pfs are generally presented as a 2-digit value. In a study, for a given processed fraction, if more than one Pf is derived, the median value is considered. In case when two Pfs are reported, no third replicate is necessary if the values do not deviate by more than 50%.

Storage stability data At the pre-harvest stage, **s**amples of RAC for residue analysis should ideally be processed immediately after harvest to ensure that its matrix remains unchanged. However, for the post-harvest uses (e.g. treatment of cereal grains while in storage), processing may be done after an interval. Here, the time gap is expected to simulate the storage time similar to the commercial storage duration. While processing an RAC, besides the fractions produced for human consumption, the by-products may also be important because of their significance for utilization in livestock feeding.

Residue definitions In general, a residue definition comprises the parent molecule and/or the key metabolites or degradation products. The definition mainly includes those metabolites (and/or degradation products) which are of toxicological concern and compounds with less than 10% of relative intensity are usually not considered for inclusion. However, the residue definition for the purpose of enforcement may deviate from the definition that is employed for risk assessment, since it focuses on the total toxicological burden (OECD 2008a, 2008b, 2009; EU Pesticide database 2016).

International scenario-processing factors

Recently, a comprehensive exercise on Pf has been published with evaluation of controlled data based on diverse kinds of processing studies (Scholz et al. 2017). The full report can be accessed on the database website which is periodically updated. Interestingly, the German Federal Institute for Risk Assessment (BfR) website has provided a graphic display of several processing operations in the form of flow charts for a quick review of the relevant information. The data sources employed for setting up the database of Pfs are based on the annual reports of the JMPR and the scientific reports published by European Food Safety Authority (EFSA).

Similar efforts to compile various processing factors have also been attempted by different countries (e.g. Australia, The Netherlands). However, the studies by the National Institute of Health and Environment of The Netherlands have reproduced the data obtained by scientific bodies such as EFSA or JMPR (National Institute for Public Health and the Environment, RIVM 2015). Subsequent to the recommendations by OECD, few researchers after a comprehensive review of the existing data on the general design of processing studies have recognized several lacunae which provide scope for further improvement (Bajwa 2014; Series on Testing and Assessment No. 96 2008).

Some of the important areas which are amenable for improvement are summarized below.

(i) One can employ a wide range (and various types) of processing operations as the international guidance documents do not specifically prescribe the details of the processing technique(s) to be employed, (ii) one can accord priority to the local processing methods, (iii) as the designations of processed fractions are non-standardized, one may combine more or less identical products/fractions into a small number of processed matrices, (iv) there is ample scope for harmonization of the categories of processed matrices and to examine the possibility of extrapolation of the processing study results to similar commodities/ processes.

Currently, comprehensive datasets have been compiled by several international authorities on the Pf of various pesticide residues in various crops and crop groups. Equipped with this global data, one can thoroughly analyze and examine the possibilities of directly adopting the Pfs in selected processed foods on a need-only basis. Although it would be interesting to understand the differences or similarities of the Pfs among different organizations, we believe this would be an elaborate exercise and would involve a thorough meta-analysis of data stemming from several organizations. There is an urgent need for initiating an exercise and establishing a compendium on processing factors which could be used to develop general guidelines ascertaining the suitability for the country.

Complexity associated with harmonization of processing factors

In general, due to a large variation in the initial residue levels in RACs, diverse nature of pesticide molecules (physiochemical properties), processing operations employed and absence of specific standard operating procedures for preparation of ready-to-eat foods, the Pfs are bound to vary depending on the RAC, pesticide and the method of preparation. These factors (wholly or in part) are applicable to internationally traded food products also. An example of such variations in the Pfs in respect of tomato and wheat are shown in Tables 2 and 3. Hence, it is rather difficult to have a common Pf, which is acceptable across the general population for any particular food. However, the median value of a number of such factors for a compound and food is normally taken for health-risk

Table 2 Processing factors in wheat products (data represent median values from different sets of experiments). *Source*: BfR database

Pesticide	Processing factors			
	Flour	Bran	Bread	Germs
Chlorothalonil	0.9–1.0	7.0	1.0	0.22
Chlorpyriphos	0.69–6.20	2.22–30.9	0.28–4.7	–
Azoxystrobin	0.25–0.84	0.38–2.8	0.13–0.67	0.5–0.81
Cypermethrin	1.25	1.20	0.55	0.31
Cymoxanil	0.50	1.20	–	–
Dithiocarbamates	0.71	2.33	0.42	1.0
Epoxyconazole	0.33–1.47	3.33–4.71	0.57–2.33	2.25–3.28
Fenpropimorph	1.14	1.44	–	–
Fluzilazole	0.17–0.65	0.14–0.43	0.65	–
Lambda-cyhalothrin	0.5	4.25	–	1.50
Tebuconazloe	0.48	0.48	–	–

Table 3 Processing factors for tomato products (data represent median values from different set of experiments). *Source*: BfR database

Pesticide	Processing factors			
	Juice	Ketchup	Puree	Paste
Cyfluthrin	0.28–0.33	0.83	0.64, 0.67	1.83
Cymoxanil	–	–	0.29	0.7
Dithiocarbamates	0.04–1.8	0.15–2.5	0.15–2.44	–
Fenpyroximate	0.5	0.5	0.67	–
Flubendiamide	0.42	–	1.83	3.79
Imidacloprid	1.47–1.52	1.53–1.89	2.86–3.0	1.82–5.4
Indoxacarb	1.5	2.42	1.60	1.08
Lambda-cyhalothrin	0.06–0.12	0.22	0.09–0.25	0.13–0.31
Spirotetramat	0.6	–	0.80	–
Tebuconozole	0.48	–	–	7.2
Thiacloprid	0.57	–	2.57	–
Thiophanate-methyl	–	1.50	2.05	–
Metalaxyl	1.0	–	2.13	–
Azoxystrobin	0.41	0.48	0.86	–
Carbendazim	1.75	5.45	6.05	–
Chlorantrinilipole	0.83	0.95	1.46	1.54
Chlorothalonil	0.09–0.32	–	0.001	0.004

assessment purposes. It involves a huge task to arrive at a consensus value, even for the regulators. Nevertheless, for dry chillies and crude oils from oil seeds, such factors have been established across the countries.

Major challenges in fixing MRLs for processed foods in India

Given the current growth of the food processing sector and the demand for processed foods and urbanization, there is an urgent need to explore the possibilities of fixing MRLs of various processed foods so as to generate the Pfs and subsequent dietary based risk analysis. The literature survey indicates that no serious attempts have been made in this direction in India till date. Recognizing the importance of this, Food Safety Standards Authority of India (FSSAI) held a two-day workshop titled "*FSSAI Workshop: Fixation of Tolerance Limits for Pesticides in Processed Food from crop commodities*" in December 2019, in which the regulatory officials, subject-matter experts, academicians and the representatives of all the other stakeholder organizations deliberated on this issue. Subsequently, recommendations were submitted to the competent authority (FSSAI 2019). The experts in the field after serious deliberations opined that this vital subject demands a careful consideration by the regulatory body.

Taking into account the diverse ramifications and complexities, we suggest that a two-pronged approach would be highly useful in addressing the issue of Pfs in processed foods in the country (see Box 1). The first approach is designated as *interim approach* and the key points are briefly presented in the upper panel. The second approach, designated as a *long term approach* would be to work out a detailed project plan (lower panel) and initiate well-designed processing studies for select processed foods which are of high priority in the country.

Broad framework/guidelines

We believe that following major steps may be adopted to address the complex exercise of fixing MRLs of pesticide residues in processed foods in India.

(a) *Compilation of Processed foods* The first step would involve listing the major processed foods in the country in the domestic market which are likely to require the Pfs for MRL fixations and quality evaluations.

- *Prioritization* This would involve a rational evidence-based approach on a priority basis. *First priority*: Focus on those processed foods which have high export value (trade); *Second priority*: Processed foods which can be designated to be of high concern, based on consumption pattern (by vulnerable population e.g., children, women and aged); *Third priority*: To identify the exclusive and locally finished (India-centric—unbranded) processed foods, which need immediate attention for assessment of pesticide residue levels (e.g. India-specific food products such as *pappad*, *namkeens*, etc.).

(b) *Compendium of processing operations* The second major step would be to establish a compendium of representative processing techniques in India which can be considered as a standard description of all relevant processes and should form a basis for validation of processing studies.

- The proposed compendium of processing techniques needs to be built upon a selection of representative and up-to-date processing studies submitted in the context of regulatory procedures for RACs.
- It should cover the most important processes in food processing, both with respect to importance in production and consumption.

Box 1 Key approaches which may be adopted in order to fix MRLs for pesticide residues in processed foods (PF) in India

(a) INTERIM APPROACH

Step 1: Adoption of processing factors*:* To adopt the existing processing factors from comprehensive databases from reliable scientific bodies such as EFSA or JMPR etc

Step 2: Ascertain their origin: To ensure that processing factors which are likely to be adopted are generated from standardized processing technologies/operations. More importantly, the processing factors should have been obtained on standardized designated processed fractions

(b) LONG TERM APPROACH

Step 1: Design/Conduct processing studies: To design/conduct well-designed experimental processing studies in order to arrive at a database of processing factors for major processed foods (in accordance with GLP standards)

Step 2: Processing studies for Specific PF: To conduct processing studies on such processed foods which have no similarity with those foods from other countries (such foods which are exclusive to the national/local consumer markets)

- For each process, a typical set of processing conditions are to be provided based on published literature and/or inquiry in the food processing industries.

(c) *Design processing studies* To design need-based processing studies for those processed foods which may be exclusive to our market on a priority basis.

(d) *Development of a database* A need to develop a comprehensive database of validated processing factors based on residue definitions for enforcement.

(e) *Grouping of processed foods* To arrive at the processing factors, fixing of MRL of pesticide residues and further dietary based health risk analysis and assessment.

Conclusion and future perspective

Internationally, the global harmonization of MRLs for pesticide residues in RACs has been well recognized and appreciated. The need to harmonize the requirements and procedures on a global platform is a prerequisite for the establishment of food standards while assessing food safety, and there exists a continuous and growing need for science-based international guidelines. Currently, in India, there is a tremendous emphasis and sustained growth in the food processing sector, and production as well as consumption of processed foods is having a rising trend. Exposure or treatments of an RAC can considerably impact and alter the residue levels of pesticides in/on the processed matrices. Depending on the processing method/s and due to the differences in physico-chemical properties of pesticides, the residue concentrations may decrease or increase in the processed fractions when compared to the original raw agricultural product. Hence, obtaining pesticide residue data from processing studies assumes importance for compliance of residues with the global legal standards and to refine dietary exposure assessment and risk to humans.

It is pragmatic that we should work towards the development of a comprehensive database of processing operations, processing studies, processing factors for various pesticides, and most importantly the extent of ‘processed food consumption’ in various groups of the general population in order to refine any possible risk associated with consumption of processed foods. To achieve this objective, it may be necessary to adopt a pragmatic approach involving both short-term and long-term strategies as discussed above. The key drivers of this exercise would be to identify the knowledge gaps regarding the risk of residues in processed foods, prioritize the foods taking into consideration the consumption pattern and trade as well as enhance the ability to protect public health and the environment.

Acknowledgements The authors would like to place on record that the deliberations during the workshop conducted by FSSAI in December 2019 in New Delhi were extremely valuable to conceptualize this paper.

Authors contribution MM: Designed the review article, manuscript writing. SM: Reviewed literature, discussed literature information. TPR: Reviewed literature, edited the manuscript. KB: Designed the review article, manuscript writing.

Funding No external funding was received to conduct this research.

Data availability All data presented in the manuscript are traceable to literature, and if required, will be made available on request.

Declarations

Conflict of interest The authors declare that they have no conflict of interest.

Consent to participate We provide consent as appropriate. We also assure that in future we will review at least three manuscripts (within our specialization) submitted to JFST.

Consent for publication We hereby provide consent for publishing the results presented in this manuscript.

Ethical approval All the authors have read and approved the submission of this manuscript. They have given consent for submission and subsequent publication of the manuscript.

References

Ambrus A, Yang YZ (2016) Global harmonization of maximum residue limits for pesticides. J Agric Food Chem 64:30–35

Bajwa U, Sandhu KS (2014) Effect of handling and processing on pesticide residues in food-a review. J Food Sci Technol 51(2):201–220

BfR (2016) http://www.bfr.bund.de (accessed on 01.02.2021)

Bren d'Amoura C, Pandeya B, Rebaa M, Ahmadd S, Creutzig SKC (2020) Urbanization, processed foods, and eating out in India. Glob Food Secur 25:100361

Codex Alimentarius (2016) Codex pesticides residues in food online database (accessed on 28.02.2021)

EU Pesticide database (2016) http://ec.europa.eu/food/plant/pesticides/eu-pesticides-database/public/?event= homepage &language=EN (accessed on 28.04.2021)

Food Safety and Standards Authority of India (FSSAI) (2019) Workshop on "Fixation of tolerance limits for pesticides in processed food from crop commodities, FDA Bhavan, New Delhi, India

Hakme E, Herrmann SS, Poulsen ME (2020) Processing factors of pesticide residues in biscuits and their relation to the physicochemical properties of pesticides. Food Addit Contam Part A 37(10):1695–1706

Heshmati A, Mehri F, Khaneghah AM (2021) Simultaneous multi-determination of pesticide residues in black tea leaves and infusion: a risk assessment study. Environ Sci Pollut Res Int 28(11):13725–13735

Holland PT, Hamilton D, Ohlin B, Skidmore MW (1994) Effects of storage and processing on pesticide residues in plant products. Pure Appl Chem 66:335–356

Industry 4.0 in Food Industry (2018) | India Food Report January 2018

Kaushik G, Satya S, Naik SN (2019) Food processing a tool to pesticide residue dissipation: a review. Food Res Int 42:26–40

Keikotlhaile BM, Spanoghe P, Steurbaut W (2010) Effects of food processing on pesticide residues in fruits and vegetables: a meta-analysis approach. Food Chem Toxicol 48(1):1–6

Law C, Green R, Kadiyala S, Shankar B, Knai C, Brown KA, Dangour AD, Cornelsen L (2019) Purchase trends of processed foods and beverages in urban India. Glob Food Secur 23:191–204

Ministry of Finance (2021) Economic survey report. http://face-cii.in/sites/default/files/food_processing_report_2019.pdf

OECD (2007) Test Guideline No. 507: nature of the pesticide residues in processed commodities- high-temperature hydrolysis, OECD Guidelines for the testing of chemicals, section 5, OECD Publishing (accessed on 28.02.2021)

OECD (2008a) OECD Guidance document on the magnitude of pesticide residues in processed commodities ENV/JMMONO, 23

OECD (2008b) Test Guideline No. 508: magnitude of the pesticide residues in processed commodities, OECD Guidelines for the testing of chemicals, section 5, OECD publishing (accessed on 28.03.2021)

OECD (2009) OECD Guidance document on overview of residue chemistry studies; series on pesticides, no. 32

OECD Test Guideline No. 508 (2008) Magnitude of the pesticide residues in processed commodities, OECD Guidelines for the testing of chemicals, section 5, OECD Publishing (accessed on 28.02.2021)

Pandey B, Reba M, Joshi PK, Seto KC (2020) Urbanization and food consumption in India. Sci Rep 10:17241

RIVM (2015) National institute of RIVM (2015) List of processing factors to evaluate pesticide residues measured in the Netherlands (accessed on 23.04.2021)

Scholz R, Herrmann M, Michalski B (2017) Compilation of processing factors and evaluation of quality controlled data of food processing studies. J Verbr Lebensm 12:3–14

Series on Testing and Assessment No 96 (2008) Guidance document on magnitude of pesticide residues in processed commodities (accessed on 28.02.2021)

Seto KC, Ramankutty N (2016) Hidden linkages between urbanization and food systems. Science 352:943–945

Yigit N, Velioglu YS (2020) Effects of processing and storage on pesticide residues in foods. Crit Rev Food Sci Nutr 60:3622–3641