Review Paper

A reassesment of the safety profile of monoamine oxidase inhibitors: elucidating tired old tyramine myths

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Supplementary tyramine data

Introductory note

Readers may note a disconnection between the abstract, the introduction, and the conclusions, in the content of the published paper, in relation to the data included on actual tyramine levels in foods from the large number of recent original references referred to in the text (which are not in the text, or the bibliography, click to skip intro and go straight to Tyr data fully detailed below).

A brief word of explanation about how this was caused by the (in)action of the journal editor is pertinent. The original agreement, in relation to the invitation extended to me to assist the journal by adding a paper to their special edition on MAOIs, was that the subject matter would be as described in the abstract. The length of the article, including references, was to be no more than 50 pages — the MS was duly delivered and no significant amendments of the scientific content of the paper by the referees reviewing it was required. However, between the various editors of the journal, and one of the referees, there was disagreement about whether the detailed tyramine data should be included, despite the fact that was expressly stated to be the intention from the very beginning (as the title states). I had suggested, at the outset, that publication of this material in an *official* online supplement* of the Journal might be a good option (a suggestion that elicited no response whatsoever).

*The absence of an *official* online supplement means that all these authors I have cited are denied the benefit of having their work cited and registered by the various databases that generate publication metrics. I can only apologize to them and point out that was entirely the decision of the editor-in-chief.

One referee opined that data should be in a table, despite the fact the text explains that would not be helpful — and I had already stated clearly that I would not put it in a table. The section editor tried to help salvage the mess, by attempting to tabulate it for them, but gave up, and agreed with what I had said from the outset, that it was neither helpful nor space-saving. Look at this paper (Andersen et al. 2018) that was published as this was 'in press' to see what I mean about tables (also, note these authors restricted their search only to Pubmed).

A more engaged and pro-active editor-in-chief would have short-circuited all this time-wasting nonsense. After all, referees are there to advise, it is rarely appropriate to allow them to 'dictate', especially about trivial issues like tables vs. lists. Editors are not what they used to be, but perhaps they never were what they used to be.

Only after a number of tedious iterations did the journal, at the last minute, tell me it was not going to have an online supplement in which to publish the Tyr material. As readers may imagine, by this stage I had expended an inordinate amount of time dealing with a journal that can only be described as being the epitome of miscommunication, chaos and indecision (almost none of the numerous communications actually elicited a coherent response, indeed, one would have to characterize that use rude and inconsiderate).

In the end I was so exhausted by all this that I removed the Tyr data and told them I would put on my own website and they could scrap the paper, or publish it as it stood, because I was not going to expend any further time or energy discussing it, or further adjusting the text: as the old saying goes it is silly to 'throw good money after bad'.

If you think the above is a long-winded explanation you should see the correspondence lying behind all of that. Let it be a warning for anybody who accepts an invitation to write a paper for a journal. Of the total time this exercise occupied only a small part of it was actually writing the paper; the rest was time wasted faffing around and discussing issues that had nothing to do with science.

Editorial competence and probity and refereeing generally is at an all-time low right across the medical science field (there would be very few authors indeed who have published in as wide a variety of different specialist Journals as I have). As the reviewer of Kassirer's recent autobiography said 'good editors get sacked' (for those who have forgotten history, he was the excellent editor of the NEJM who was sacked in 1999).

Never again. I get wider exposure 'publishing' on my own website, so why waste time with dysfunctional profit-greedy journals? They get scientists to do most of the work and their profit-margins are higher than any of the top 500 listed companies. Parasites, yes; added value, no.

The text below is exactly as it was in the full version of the paper.

That text was scrutinized by several reviewers for the journal. Thus, it is 'peer reviewed' — for what that is worth. One of the reviewers opined that decarboxylating enzymes could never survive cooking because that involved temperatures of 150-200°C! Many will sympathise with my initial response, which was to say I would politely decline an invitation to dinner at his house. That is but one (at least slightly amusing) example from a number of 'unhelpful' comments. But it is a disappointing reminder of the lack of knowledge about these matters, even among supposed experts, selected by a reputable journal, to do reviewing for them.

> As Dr. Johnson might have said: The comments on this manuscript were both relevant and correct. Unhappily, the correct ones were not relevant, and relevant ones were not correct.

General comments on diet and tyramine

> 'The pleasures of the table belong to all men and to all ages, and of all pleasures remain the last, to console us for the passing of the rest.'
> Anthelme Brillat-Savarin

This review is of Tyr concentrations, as indicated by a large recent body of food science research, which has not previously been cited in the medical literature.

Tyr can only accumulate to higher concentrations in ordinary (i.e. non-fermented) foods as a result of contamination (with decarboxylating organisms), combined with excessive storage time and temperature (>4°C). This is especially relevant to things like liver and liver pâtés, where extra care should be taken with domestic refrigerators which do not always maintain items at <4°C, Modern commercial food hygiene and handling practices and regulations in most countries mean that excess Tyr levels are rare in 'fresh' foods. That leaves those foods that are produced using micro-organisms; that is the subject-matter of the major part of this review.

Minimising or avoiding the few high Tyr foods and beverages that do exist can be reliably achieved and remains necessary whilst taking MAOIs. Only a few foods can build up the degree of excess Tyr (hundreds of mg/kg) that can greatly raise the BP. A pressor response is in proportion to the amount of Tyr that is consumed: i.e. it is a dose-related effect. That is why it is permissible and safe to cautiously test small quantities of some foods e.g. a favourite cheese or soy sauce.

This review cannot deal individually with compound foods, e.g. pizza. Such foods can have various ingredients with different Tyr content. Most pizza styles use mozzarella cheese, which has no Tyr, although other cheese styles may be used (cheddar, Edam etc.): these are 'commercial' styles that are stored frozen and are highly unlikely to be high in Tyr (Ma et al. 2014). Such considerations illustrate why simple tables and lists of 'prohibited' foods are of limited use and why the advice and knowledge of an informed physician is required.

Special starter-cultures that are deliberately 'engineered' to have no decarboxylating micro-organisms in them, and therefore produce no Tyr, have been developed and are now used in almost all food production processes. They are used by most cheese-makers (including 'artisan' makers) because they also minimise the formation of undesirable 'off' flavours. Furthermore, they minimise the proliferation of contaminant organisms and thereby further lessen any chance of Tyr formation. Worldwide, attention has focussed increasingly on 'food hygiene' and the European Union have an extensive program of monitoring and research.

Seminal early research on the Tyr content of cheeses was done by Kosikowski. Those papers have never been cited in the medical literature, except by Blackwell (Blackwell and Mabbitt 1965; Kosikowski 1954). Blackwell noted that almost all cases of the 'cheese reaction' then reported (1965) implicated cheddar cheese, some of which had been assayed as having around 3,500 mg/kg of Tyr (Bullock and Irvine 1956), which exceeds, by two orders of magnitude, the values generally found in similar cheeses in the current era.

In the past doctors have been dogmatic about instructing patients to completely avoid certain foods. Patients inevitably consume them sooner or later, and because most of them are not high in Tyr and cause no reaction, they then conclude that doctors are exaggerating which may lead to subsequent carelessness about diet. It is important for doctors to explain things accurately to patients, which they cannot do if they do not know the facts themselves.

Dairy products

Cheese: 'Milk's leap toward immortality'
Clifton Fadiman

Most cheeses now have low Tyr levels (<10 mg/kg), whether they are hard, semi-hard, acid-curd or soft (Bunkova et al. 2010; Fiechter et al. 2013; Linares et al. 2012; Mayer et al. 2010; Palermo et al. 2013; Spizzirri et al. 2013). Thus, one can confidently state that most cheeses will not cause any reaction in a patient on a fully effective dose of an MAOI — this is why it is important to explain the situation properly to patients and not to dogmatically assert that all cheese is prohibited.

There have been thousands of Tyr estimations performed from cheeses all over the world: a selection of studies with extensive and varied sampling is given here to illustrate this.

Almost all commercial lower priced 'processed' and 'supermarket' cheeses are low in Tyr (always <200 mg/kg, usually in the range of 0-50 mg/kg). A 'diet-conscious' serving is 25 g, 50 g is a large serving. Thus, a 50 g serving of 50 mg/kg would have only 2.5 mg of Tyr. 'Supermarket' type outlets require low prices and industrial-scale quantities of produce: low prices do not pay for long warehouse ageing (i.e. more than 3 months). Bunkova et al. examined the widely marketed Edam-style cheese and studied Tyr levels during maturation: they found a maximum, after 100 days, of 120 mg/kg in the rind and 70 mg/kg in the core (Bunkova et al. 2010).

Matured and 'artisanal' cheeses can, but only rarely, develop high concentrations of Tyr (~1,000 mg/kg), although most are surprisingly low. 'Matured' usually means aged for more than 3 months, rather than just a few weeks. A 25 g serving of a cheese of 1,000 mg/kg would have 25 mg of Tyr, which would still not be likely to precipitate a marked pressor response for the majority of people taking MAOIs.

Classic matured (hard and semi-hard) cheeses

French

Francophiles may be surprised to be reminded that there are relatively few French hard cheeses and even fewer that are available outside France, examples are: Cantal, Comté, Emmental (generally produced industrially) and Mimolette (Edam-like).

Comté is still mostly in the hands of small producers, whereas the similar Swiss Gruyere is almost entirely produced by large-scale co-operatives: Mayer, 0 mg/kg (Mayer et al. 2010).

Italian

Parmigiano Reggiano: aged 24-30 months, 20-150 mg/kg (Spizzirri et al. 2013), but Mayer (Mayer et al. 2010) found levels <10 mg/kg in the 6 samples tested.

Grano Padana, 12-22 months old) all samples Tyr <130 mg/kg (Spizzirri et al. 2013). Mayer (Mayer et al. 2010) found undetectable levels.

The Spizzirri paper included a wide range of cheeses (mostly Italian), Grana Padano, Pecorino, Provolone, Ripened goat cheese, Emmentaler, Taleggio, Bel Paese and more, none of which had more than 200 mg/kg of Tyr.

In a wide variety of Italian pecorinos, made from all the different significant producing regions of Italy, some very 'artisan' type cheeses, there was great variation. Many have quite low levels in the region of 100-200 mg/kg, but one particular example, Pecorino Del Parco Di Migliarino San Rossore, exceeded 1000 mg/kg (Schirone et al. 2012).

British

Cheddar: young cheddar (4 weeks) all samples <50 mg/kg, at 36 weeks maturation, all samples <160 mg/kg (Rea et al. 2004). This is two orders of magnitude less than the old value of around 3,700 mg/kg of Tyr (Bullock and Irvine 1956; De Vuyst et al. 1976).

Dutch

Gouda is a very widely copied cheese style which when young is semi-soft and hardens with age. Tyr levels increase a little on aging, younger ones mostly <50 mg/kg (Komprda et al. 2008a;

Komprda et al. 2008b), older ones 100-250 mg/kg (Mayer et al. 2010).

Swiss

Gruyere: <100 mg/kg (Spizzirri et al. 2013). Emmental: 0-68 mg/kg (Mayer et al. 2010), and 16 mg/kg (Spizzirri et al. 2013).

Other cheeses (non-hard)

Washed and unwashed rind

Normally these cheese styles (Brie, Camembert etc.) are only matured for 4 weeks and all now use starter-cultures. Tyr levels of <10 mg/kg are the rule. Examples from Austria, Denmark and France found negligible Tyr levels (max 5 mg/kg) in 5 different types (Mayer et al. 2010). Older papers found Tyr ~100 mg/kg (Asatoor et al. 1963; Horwitz et al. 1964); but Kosikowski (Kosikowski 1954) found undetectable levels.

Other cheese types

Acid-curd cheeses: some are coagulated (curdled) using rennet, but some undergo curdling by bacterial lactic acid fermentation. 'Ripened' examples of these can contain Tyr of up to 500mg/kg, although most contain a lot less: out of 47 samples the median Tyr was determined at 30 mg/kg (but one 'Tyrolean Graukäse' had 1,600 mg/kg). (Fiechter et al. 2013).

Feta style: generally low Tyr but 'older' examples, max 250 mg/kg at 120 days of age (Valsamaki et al. 2000).

Roquefort and Roquefort styles

Roquefort and Roquefort style 'traditional' cheeses (all made with Penicillium Roqueforti): Roquefort 4 samples, Tyr 0 mg/kg (Mayer et al. 2010).

Czech blue cheese: Tyr average 380 mg/kg, different cheeses (vats) varied widely, from 10 mg/kg, to 875 mg/kg (Komprda et al. 2008c; Novella-Rodriguez et al. 2003).

Non-matured cheeses, yogurt, milk

Cheese spreads

These occupy an in-between position, it depends on what they are made from: some higher quality cheese spreads are made from vintage cheeses, a few of which may be relatively high in

Tyr. As an example, 'Parmareggio' cheese spread had Tyr 40 mg/kg (Spizzirri et al. 2013). Most spreads are like commercial cream cheeses and contain no Tyr.

Unripened cheese styles

Fresh non-matured, i.e. unripened/unaged, cheese styles, and yoghurt, are always safe because milk itself has no Tyr: e.g. curd styles, fromage frais, mascarpone, cream, ricotta, mozzarella, cottage cheeses, bocconcini (Novella-Rodriguez et al. 2002; Novella-Rodriguez et al. 2000; Spizzirri et al. 2013).

Milk and yogurt

Yoghurt 0 mg/kg (Gezginc et al. 2013; Novella-Rodriguez et al. 2000). Korean Yoghurt, 8 samples, max of 4 mg/kg (Cho et al. 2006).

Fermented vegetables and cereals

Sourdough bread

In the modern world the most prominent cereal-related solid-food vestige of these ancient fermentation practices is sourdough bread. Özdestan has investigated various Turkish examples and a minority do have some Tyr: like kumru (ten samples from different manufacturers in Turkey) < 5mg/kg, shalgam (20 samples) < 50 mg/kg, and tarhana (20 samples) 50-100 mg/kg (Ozdestan et al. 2012; Ozdestan and Uren 2011).

Marmite, Bovril, Promite, Vegemite

Marmite is made from the residual brewer's yeast. It may have relatively high amounts of BAs ~320 mg/kg of Tyr (Populin et al. 2007) and 650 mg/kg of Tyr (Shulman et al. 1989). Both those are rather less than Blackwell's original estimate (Blackwell et al. 1969; Blackwell and Marley 1965; Blackwell et al. 1965) of around 1,500 mg/kg. Marmite-like spreads are somewhat similar to soy sauces and 'miso' which also involve 'fermentation' of brews containing vegetable proteins. They are usually used in small amounts, which can be safely eaten. A teaspoon (5 ml) of 'Marmite" would have only 5/1000 x 300 mg, i.e. only a couple of milligrams.

Soybean products

All *fermented* soybean products like sauces and pastes may have significant Tyr levels. Non-fermented products like (most) tofu have no Tyr (Toro-Funes et al. 2015).

Tyr is produced slowly during the fermentation of soy sauces, natto, miso and sufu etc., reaching typical concentrations of ~150 mg per kg (litre) after many months.

Japanese soy sauces: most samples measured have ranged between 10-200 mg/L (Ibe et al. 2003). Maximum Tyr concentrations in the past may have been as high as 1000 mg/L, so 25 ml of that would have contained 25 mg of Tyr (Guidi et al. 2012; Kim et al. 2012; Shukla et al. 2011).

Most supermarket soy sauces actually have Tyr levels around 100 mg/L. Hundreds of samples have been assayed, all had Tyr <200 mg/L (Stute et al. 2002; Yongmeia et al. 2009).

Miso soup and sufu: 40 samples: all <50 mg/L (Kung et al. 2007a; Kung et al. 2007b:Cho, 2006 #9846). 'Natto' is another fermented soybean preparation that sometimes achieves high Tyr levels, although <100 mg/kg is typical (Kim et al. 2012; Tsai et al. 2007).

Fermented sauces: animal

Fish sauces

They vary with producer and hygiene quality, but seem usually to be fairly low, 200-500 mg/kg (Cho et al. 2006; Stute et al. 2002). Worcestershire sauce is similar. If used in 'condiment quantities' (<25 ml) they are unlikely to be a problem (viz. 25 ml of 500 mg/kg mg would have 12 mg of Tyr).

Meat and fish

Fresh and frozen meat and meat products are safe, but if they are not fresh, i.e. if they have been subject to action by micro-organisms, then they can be problematic. Fresh liver has no Tyr (Krausová et al. 2006), but if stored badly may develop significant levels (Boulton et al. 1970; Hedberg et al. 1966). The Hedberg paper is an illustration of good observation and investigation.

Sausages, pâtés, meat pastes, preserved meats

These have minimal Tyr unless poorly prepared or stored (Curiel et al. 2011; Delgado-Pando et al. 2012; Ruiz-Capillas and Jimenez-Colmenero 2010).

Dry-cured meats

As with all *dry-cured* meat products (as opposed to fermented ones) only low concentrations of Tyr are expected, <5 mg/kg. Parma ham, pastirma, jamon, prosciutto, coppa etc. will all be safe (Lorenzo et al. 2007; Ruiz-Capillas and Jimenez-Colmenero 2004).

Fermented sausages

Concentrations of Tyr depend, as shown by the data on cheese, on the hygienic quality of the meat used and the strains of bacteria involved in the fermentation process. The widely used starter-cultures are engineered to have no decarboxylase activity which results in much lower concentrations of BAs, including Tyr (Bover-Cid et al. 2009; Gardini et al. 2008; Latorre-Moratalla et al. 2010; Latorre-Moratalla et al. 2012; Latorre-Moratalla et al. 2008; Leggio et al. 2012).

Numerous studies from all over Europe have found Tyr was usually below 200 mg/kg, very few samples were as high as 600 mg/kg (Bover-Cid et al. 2001; Komprda et al. 2001; Papavergou et al. 2012; Ruiz-Capillas and Jimenez-Colmenero 2004; Suzzi and Gardini 2003).

Hygiene and low temperature processing continue to improve steadily, more recent surveys find generally lower concentrations (Ferreira and Pinho 2006; Latorre-Moratalla et al. 2008; Miguelez-Arrizadoa et al. 2006).

Stock cubes, gravy powders, bouillons

These are not prepared by fermentation but are flavoured extracts and reductions, therefore they are most unlikely to be high in Tyr. Populin et al. tested broths (homemade or canned products from the market), soups (ready-to-eat soups, condensed soups and creams), soup bases (bouillon cubes, pastes and granulated powders), and sauces from the European and US markets: none exceeded Tyr 10 mg/kg (Populin et al. 2007).

Fish

Cured fish

Various types of fish (especially salmon) are 'cooked' using food acids (cf. pickling). The most widely known dish using this technique is Gravlax, fresh hygienically prepared fish done in this manner has low Tyr.

Smoked & dried fish

Cold smoked salmon, Tyr <20 mg/kg (Jørgensen et al. 2000). Dried salted Tuna roe, Tyr was 90 mg/kg (Periago et al. 2003).

Canned fish

Some canned samples reach Tyr 10 mg/kg, but that seems rare: max 70 mg/kg (Veciana-Nogues et al. 1997; Veciana-Nogues et al. 2006).

Vegetables and fruits

Vegetables generally have total BA concentrations of only a few mg/kg and Tyr levels of about 0.2 mg/kg with a maximum of 1 mg/kg (Moret et al. 2005), but can these increase a little with spoilage.

Plants do produce a large range of amines and psycho-active alkaloids, the concentration varies greatly depending on many factors like plant variety, tissue type, stage of growth and attack by other organisms etc.

Useful reviews are: (Kalac et al. 2002b; Lavizzari et al. 2006; Ly et al. 2008; Moret et al. 2005). It has recently emerged that some of these compounds affect TAA receptors and TRP channels e.g. capsaicin, menthol (Calixto et al. 2005).

Avocado and banana

There is one credible report of high BP after consumption of about six avocados, probably over-ripe (Generali et al. 1981). There are no recent data on Tyr levels. However, see below, it is possible for fruits to produce such amines, and large quantities of rotten fruit (browned/blackened) may accumulate sufficient dopamine to cause a rise in BP. The fact that there have been no further reports in forty years indicates it is pretty difficult to ingest significant or problematic amounts via fruits.

Bananas contain dopamine, up to 400 mg/kg in the pulp, about 1,500 mg/kg in the skin (Quansah 2009), but probably little Tyr (Lavizzari et al. 2006; Riggin et al. 1976). Although DA cannot cross the BBB (Martel et al. 1996), plasma DA may be elevated, and raised peripheral DA may raise BP by vaso-constriction.

Normal servings of fresh vegetables, fruits etc. are unlikely to have any problematic adverse effects via histamine, Tyr or L-dopa (that includes broad-beans, aka fava beans, and related species).

Fava (faba) beans

Fava beans (*Vicia Faba*, aka broad beans) have Tyr at about 10 mg/kg (Moret et al. 2005), and low concentrations of L-DOPA. That is not sufficient to have any significant effect even in large serving sizes.

Sauerkraut

Sauerkraut is made by lacto-fermentation: a review of more than 100 samples from 7 countries, all had Tyr <200 mg/kg, except a couple from Czech Rep. which were 400-900 mg/kg (Kalac and Glória 2009). Korean 'kimchi' cabbage averaged 50 mg/kg, max 120 mg/kg (Cho et al. 2006).

Chocolate

Chocolate sometimes involves a short fermentation stage. A few recent papers have added data on dozens of samples of cacao powder, chocolate (white, milk, dark) and syrup, none of which exceeded 35 mg/kg, most being <10 mg/kg (Restuccia et al. 2016; Restuccia et al. 2015). Other results are in the same range: (Baker et al. 1987; Baranowska and Płonka 2015; Granvogl and Schieberle 2007; Lavizzari et al. 2006; Mayr and Schieberle 2012; Pastore et al. 2005; Spizzirri et al. 2016).

Health & sport supplements

These substances contain all sorts of additives, many of them are potentially injurious (phenethylamine, synephrine, hordenine, *β*-methylphenethylamine, *N*-methylTyr, octopamine and deterenol). These were identified from 32 dietary supplements sold in the US market. Their listing of the ingredients may be unreliable. Some definitely do contain Tyr at levels of up to 7 mg per 'recommended serving' (0.7 mg/g) (Gatti et al. 2012; Koh 2017; Zhao et al. 2018).

Wines, spirits and beers

A meal without wine is like a day without sunshine.
Anthelme Brillat-Savarin

Wines and beers in moderation (two drinks in 2 hours) are safe (as far as Tyr is concerned). Modern hygienic production methods have made Tyr concentrations >10 mg/L rare (but cf. 'lambic' beers).

Tyr in liquids taken on an empty stomach should be regarded as a special case, because Tyr will be absorbed much more rapidly (Berlin et al. 1989; VanDenBerg et al. 2003), so amounts of Tyr of one third of the figures given above may provoke a modest pressor reaction. One small (330 ml) glass of some 'live' beers could, in *rare* instances, have about 10 mg of Tyr; this is sufficient to cause a pressor reaction in a minority of people, e.g. see (Bieck and Antonin 1988; Ottervanger et al. 1993).

Wines

Here with a loaf of bread beneath the bough,
A flask of wine, a book of verse - and thou
Omar Khayyam

Wines do, if only rarely, contain some Tyr, but at levels that are safe unless wine is consumed in excess.

Recent major reviews have covered many hundreds of different wines of all types: almost all have had Tyr levels of less than < 5 mg/L (Ancin-Azpilicueta et al. 2008; Arrieta and Prats-Moya 2012; Ginterova et al. 2012; Gomez-Alonso et al. 2007; Henriquez-Aedo et al. 2012; Hlabangana et al. 2006; Jayarajah et al. 2007; Konakovsky et al. 2011; Lonvaud-Funel 2001), also aged and fortified wines, all Tyr <5 mg/L (Mafra et al. 1999; Moreno-Arribas and Polo 2008).

Wines: 300 samples max Tyr <5 mg/L (Landete et al. 2005; Leitao et al. 2005).

Sixty-one different Spanish wines including aged Rioja Gran Reserva: Tyr range 0-11.32 mg/L, Average 1.40 ± 2.35 mg/L (Marcobal et al. 2005).

The repetition of the notion that Chianti, uniquely amongst wines, contains significant concentrations of Tyr (Horwitz et al. 1964), illustrates that many reviewers have been careless about the relevance and reliability of their sources of information, and ignorant about winemaking and Tyr formation. The chianti error, besides being highly implausible, was disproved 40 years ago by an eminent research group and published in the Lancet, no less (Hannah et al. 1988). Yet this myth continues to be repeated *ad nauseam*, illustrating the ongoing poor research and scholarship which bedevils this field.

Beers

Shulman's group (Tailor et al. 1994) looked at a total of 98 beer samples, from 79 different brands of beers, in 1994: that is but the tip of the iceberg.

Most, but not all, standard commercial and modern beers all over the world will be safe (<10 mg/L) in moderation; some low volume 'artisan' and 'boutique' beers are a little more likely to be problematic (including non-alcoholic beers). Beers made using natural yeasts (spontaneous fermentation) rather than starter-cultures, are more likely to have contaminants and therefore more Tyr. This is an observation echoed throughout this review with all types of 'fermentation', whether with cereals or sausages.

One review looked at 195 samples from Germany, Austria, Belgium, Bulgaria, Czech Republic, Denmark, Spain, France, Great Britain, Greece, the Netherlands, Ireland, Italy, Portugal, Switzerland, and Yugoslavia. They found a great majority were low (2-8 mg/L, mean 7), but a few are up to 30-50 mg/L, with a maximum of 70 mg/L (Izquierdo-Pulido et al. 1996; Kalac et al. 1997; Kalac and Krízek 2003; Kalac et al. 2002a).

Bunka reviewed 114 samples (Buňka et al. 2012) and Tyr was <10 mg/L in 51 samples, between 10 and 50 mg/L in 21 samples and 100 mg/L in 5 samples. This included 16 non-alcoholic beers, several of which had around 50 mg/L.

Pradenas et al. in Chile assayed over 100 types and found 99% of 316 beer samples were no more than 2 mg/L, one was 6 mg/L (Pradenas et al. 2016).

China: 18 beers, some European brewed under licence, values mostly Tyr 3-5 (max 7) mg/L (Tang et al. 2009).

Belgian beers especially can have high Tyr, out of 220 samples, 21 had Tyr at 28 mg/L, and the maximum was nearly 70 mg/L (Loret et al. 2005). A single normal serving (330 mL) could have 10 mg of Tyr and, on an empty stomach, be sufficient to cause at least a minor pressor episode.

Belgian 'lambic' beer is a good exemplar of the general principles: it is an old style allowed to spontaneously ferment with wild airborne yeasts (therefore more likely to contain 'contaminant' organisms with decarboxylating activity) and then aged for 1-3 years.

This large number of assays indicate that a great majority of beers are very low in Tyr, but beers from 'micro-breweries', open fermented or 'live' beers, or exotics like Belgian lambic, may need testing carefully.

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