

## Monoamine Oxidase Inhibitors (MAOI), Tyramine and Drug Interactions (Abbreviated)

Dr P Ken Gillman V.abbrev.3.1 2016

### Key Facts

- For people who already follow healthy eating (and drinking) amounts a low tyramine diet involves few changes
- Only some foods that are past their shelf-life or 'off', or those prepared using maturation and 'fermenting' techniques, can *sometimes* have high tyramine
- The increased blood pressure reaction that can result from excess tyramine ingestion is proportional to the amount of tyramine ingested
- Very few foods or drinks have tyramine levels sufficiently high that a small amount (i.e. 50 grams or ml, or less) is *likely* to cause a risky degree of hypertension
- Modern cheeses are safe in healthy-sized portions. Only a few mature or aged cheeses can *sometimes* have higher tyramine concentrations, so care and awareness is needed
- If a reaction occurs the chance of coming to serious harm is remote
- The symptoms of a reaction are: a thumping forceful heartbeat (usually a **slower** than normal pulse rate), paleness (pallor), rapid onset severe headache, tightness in the chest. Pulse may drop as low as 40 beats per minute
- The wide variability of sensitivity to tyramine between individuals means that a small percentage of people may notice reactions with smaller doses
- It is a good idea to monitor blood pressure
- Double-check the compatibility of medications: see below
- There are few over-the-counter drugs that are a problem, because the ephedrine type drugs (with **indirect sympatho-mimetic activity [ISA]**) have been taken off the market (in many countries). Drugs with significant ISA activity (see below) may be risky.

### General Summary

This is an abbreviated version of the full monograph (17,000 words, 350 references) which may be studied by those requiring more detailed information. It has details of the tyramine content of a large range of foods and detailed explanations of drug interactions.

Interactions between **monoamine oxidase inhibitors (MAOI)** and other drugs are now well understood (1) and there is more data on the tyramine in foods, and also on how much is likely to constitute a problem (2).

Concentrations are given as milligrams (mg) of tyramine per kilogram (kg) or litre (L).

**For those who already follow healthy eating amounts and patterns an MAOI low tyramine diet involves almost no changes at all.**

There is considerable variation of tyramine sensitivity between different people. Therefore, a small proportion of people may get a blood pressure increase with only 10 mg of tyramine, but most people need to have 25 - 50 mg (in a meal) to get a blood pressure reaction. For a detailed analysis of the evidence relating to tyramine dose and blood pressure see the full monograph, and (1).

Learn what 10 g or 100 g of cheese looks like. Healthy amounts of cheese are around what is safe tyramine-wise: few contain more than 25 mg/100 grams, so a 25 gram (i.e. a healthy) portion contains only 6 mg of tyramine and that is not a problem, even in tyramine-sensitive individuals.

Monitor blood pressure while on MAOIs: buy a \$50 BP monitor (upper arm, not the wrist or finger type which are rather less accurate).

Even if excessive tyramine is ingested and BP increase occurs, serious consequences are very unlikely providing appropriate action is taken. That will usually mean nothing more than monitoring blood pressure for a 2-3 hours. Hasty treatment of high BP by inexperienced doctors risks doing more harm than good and it should only be undertaken in hospital (1, 3). Sub-lingual nifedipine is strongly advised against, do not use it: see full monograph for details of advice re treatment of hypertensive episodes (urgencies). There is a PDF about blood pressure monitoring (menu on left of web site page). There are two reasons for BP monitoring:

- 1) variation in the population: some people will get more marked reactions of BP elevation with relatively smaller doses of tyramine. It will tell you if you are tyramine sensitive and alert you to the need to be extra careful about diet
- 2) BP drop on standing is the best measure of the effectiveness of a given dose and essential to optimal speed of adjustment to the final effective dose.

## **Introduction**

These drugs are called **Mono-Amine Oxidase Inhibitors (MAOIs)**. This covers both food and drink, and drug interactions, for those taking MAOIs.

Keep some means of identifying the fact that people are on MAOIs, like with insulin/epilepsy.

Advice on MAOIs should ideally come from specialist psychopharmacologists, most general psychiatrist have insufficient knowledge to manage MAOIs optimally.

I have published various papers on the pharmacology of MAOIs and their interactions, see: (1, 4-11).

## **Tyramine**

Tyramine formation in foods requires the presence of micro-organisms with amino acid decarboxylase enzyme activity. Modern food production

Dr Ken Gillman [kg@matilda.net.au](mailto:kg@matilda.net.au)

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techniques have mostly eliminated such bacteria from the food supply chain. Tyramine increase has a lot to do with 'freshness' (i.e. time and storage conditions).

### Symptoms of Blood Pressure Reactions?

A reaction is an increase of BP over 30 - 60 minutes and usually shows first as a forceful thumping heartbeat. Pulse usually becomes **slower** (12). If blood pressure goes up to 180 mm Hg or more severe headache is usual. Tightness in the chest, paleness (pallor) may occur. Symptoms may last for about two hours.

### Tyramine in Foods and Beverages

Few foods, except cheese, have high tyramine and any BP reaction is proportional to the amount that is consumed: it is a dose-related effect.

For detailed data on particular foods etc. see full monograph.

## Cheeses

Most cheeses now have low tyramine levels (< 10 mg/kg), whether they are hard, semi-hard, acid-curd or soft (13-18), which includes almost all commercial lower priced "processed" and "supermarket" cheeses whose tyramine levels are <200 mg/kg, usually in the range of 0 – 50 mg/kg), Budget prices do not pay for long warehouse ageing (i.e. more than 3 months).

### Brie and Camembert styles

Normally these are only matured for 4 weeks before release, so low tyramine levels are expected. Mayer et al looked at examples from Austria, Holland and France and found maximum tyramine levels of 85 mg/kg with undetectable levels in many examples (14).

### Matured Cheeses

Parmigiano Reggiano, aged 30 months, tyramine 20 – 150 mg/kg (16).

Cheddar, tyramine < 50 mg/kg, at 36 weeks maturation all samples < 160 mg/kg (19).

Gouda, tyramine 100 – 250 mg/kg (14).

Gruyere, tyramine < 100 mg/kg (16).

Emmental, tyramine 0 - 68 mg/kg (14).

### Non-Matured Cheeses, Yogurt

Unripened cheese styles: no tyramine, e.g. curd styles, *fromage frais*, mascarpone, cream, ricotta, mozzarella, cottage cheeses, *bocconcini*.

Mozzarella, Ricotta. Multiple samples, tyramine, 0 mg/kg (16). Milk and yoghurt: no tyramine.

### Marmite, Bovril, Promite, Vegemite etc.

It is likely that changes in the way these products are prepared in recent years have lowered the tyramine content; level ~ 320 mg/kg of tyramine

Dr Ken Gillman [kg@matilda.net.au](mailto:kg@matilda.net.au)

<http://www.psychotropic.com/anti-depressants/maois>

(20). A teaspoon of 'Marmite' would have at most 5/1000 x 300 mg of tyramine, i.e. only a couple of milligrams.

### Soy sauce

Most supermarket Soy sauces actually have only around 100 mg/L. Yongmeia (21), 40 samples of Chinese soy, mostly less than 200 mg/litre (20 of the 40 were < 100 mg/kg). Normal quantities (10 – 20 mls) are safe.

## Meat and Fish Products

Fresh and frozen meat and meat products are safe. Fresh liver has no tyramine (22). Similarly, liver pate (and similar meat or fish pastes) are safe if freshly made and properly refrigerated.

### Meats, Preserved

Dry cured products: Parma ham, prosciutto etc are safe. Papaverkou max 15 mg/kg (23).

### Fermented sausages

Improved starter cultures result in much diminished tyramine content (24-27).

Most salami types are < 100 mg/kg.

## Pizza

It depends what you put on it. It is clear from the data (see full monograph) that commercial pizzas are likely to be safe (mozzarella has no tyramine), as found by Shulman (28). Gourmet pizzas may contain mature salami and cheese with higher tyramine concentrations, but the quantities are likely to be small so the total tyramine load is unlikely to be problematic.

## Wine and Beer

Wine is safe. Modern hygienic production methods have made excessive tyramine concentrations rare (in both wine and beer). A little caution is warranted with 'boutique' and open fermented beers, rare examples can be high.

## MAOIs: Interactions with Other Drugs

Myth: MAOIs have many dangerous interactions with other drugs.

Yet there are only two interactions: just SRIs and ISAs.

The potentially risky interactions with MAOIs are:

1. Serotonin syndrome, caused by (S)SRIs + MAOIs
2. Blood pressure elevation, caused by tyramine in food, or by the other '**indirectly acting sympatho-mimetic amines (ISA)**' (releasers) like ephedrine & pseudoephedrine.

Dr Ken Gillman [kg@matilda.net.au](mailto:kg@matilda.net.au)

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## Anti-Depressant Drugs

Any drug that works as a serotonin reuptake inhibitor (SRI) is potentially dangerous (possibly fatal) if combined with an MAOI (5, 29) including: sertraline, fluoxetine, paroxetine, fluvoxamine, citalopram, escitalopram, clomipramine or imipramine, or SNRIs like milnacipran, venlafaxine, desvenlafaxine, duloxetine.

NB It is usually stated that all TCAs pose a risk, but that is definitely not correct, it is **only clomipramine and imipramine**.

On ceasing other antidepressants to start MAOIs, washout intervals varying between one and five weeks may be required. No washout is required for TCAs (other than clomipramine and imipramine), or mirtazapine, mianserin, trazodone or reboxetine, because they are safe taken together with MAOIs.

## Risky Analgesics

The risk is that of serotonin toxicity (ST), because some act as SRIs, as explained in detail in my review (11), pethidine (aka meperidine) and tramadol, especially, are a significant risk for anyone on MAOIs.

Dextromethorphan, (dextro)propoxyphene and pentazocine are also best avoided.

It is safe to have an anaesthetic whilst on MAOIs.

## Ceasing Treatment

This advice on diet and possible interacting drugs should be followed for a minimum of two weeks (six weeks in some situations) after ceasing MAOIs (between one and three days in the case of moclobemide).

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Dr Ken Gillman [kg@matilda.net.au](mailto:kg@matilda.net.au)

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Dr Ken Gillman [kg@matilda.net.au](mailto:kg@matilda.net.au)

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Dr Ken Gillman [kg@matilda.net.au](mailto:kg@matilda.net.au)

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Dr Ken Gillman [kg@matilda.net.au](mailto:kg@matilda.net.au)

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