CNS Drugs (2013) 27:789–797
DOI 10.1007/s40263-013-0097-3

LEADING ARTICLE

Current Place of Monoamine Oxidase Inhibitors in the Treatment of Depression

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Published online: 10 August 2013

Abstract This paper reviews the discovery and history of the use of irreversible monoamine oxidase (MAO) inhibitors (MAOIs) such as phenelzine, tranylcypromine and isocarboxazid, as well as the second generation selective and reversible MAOIs such as the MAO-A inhibitor, moclobemide and the MAO-B inhibitor, selegiline. Data for review were identified from a literature search of OvidSP Medline and PsycInfo performed in July 2012, using the subject terms and keywords of 'monoamine oxidase inhibitors', 'major depression', 'depressive disorder' and 'depression (emotion)'. The search was limited to papers published in the English language and from 2007 onward only.

Irreversible MAOIs have the potential to treat the most challenging mood disorder patients including those with treatment-resistant depression, atypical depression and bipolar depression. Unfortunately, the use of irreversible MAOIs has been declining sharply due to lack of marketing and the excessive fears of clinicians. Moreover, few clinicians now have any experience, let alone comfort, in prescribing this class of antidepressants. The newer MAOIs are available as another option for the treatment of major depression but have not replaced the irreversible MAOIs for the specific sub-types of depression for which they are now recommended in most consensus guidelines and treatment algorithms.

The pharmacology, drug interactions and dietary recommendations associated with the use of MAOIs are reviewed. With the appropriate dietary restrictions and attention to potential drug interactions with serotonin and noradrenaline agents this class of drugs can be used effectively and safely. The MAOIs still represent an important element in our therapeutic armamentarium. Despite recommendations by opinion leaders and consensus guidelines for the use of MAOIs in specific sub-types of depression, the prescription rate of MAOIs is far less than expected and is decreasing. The "bad reputation" and the lack of industry support for this class of agents (especially the irreversible MAOIs) must be overcome in order to continue to provide a potentially useful treatment for a very vulnerable yet substantial sub-population of mood disorder patients.

1 Historical Background of Irreversible Monoamine Oxidase Inhibitors (MAOIs)

As in many discoveries in psychiatry, the use of irreversible monoamine oxidase (MAO) inhibitors (MAOIs) began by serendipity. In the early 1950s, the antitubercular agent iproniazid—a derivative of the hydrazine compound isocarboxazid—was found to have antidepressant effects in tuberculosis patients who suffered from depression [1]. Following this discovery, the MAOIs were used as the first effective antidepressants and by 1957 Nathan Kline published the first report on the neuropsychiatric experiences with iproniazid calling it a "psychic

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energizer". Within a year of that report more than 400,000 depressed patients were treated with this drug marketed as Marsilid [2].

Shortly after iproniazid was discovered to have antidepressant properties it was also found to inhibit the enzyme MAO, which is involved in the catabolism of serotonin, noradrenaline and dopamine [1]. In association with the discovery of tricyclic antidepressants (TCAs), this led to the formulation of the monoamine theory of depression. Moreover, the discovery of an "antidepressant drug" such as iproniazid had a profound effect on the overall attitude towards clinically significant depression by emphasizing its underpinnings as a "chemical imbalance" [2]. Over subsequent decades, antidepressants with a wide variety of monoamine-based mechanisms of action were developed. Iproniazid was eventually removed from the American market because of hepatotoxicity, but was followed by the discovery of more potent inhibitors of MAO, which were more effective antidepressants including phenelzine (Nardil), isocarboxazid (Marplan) as well as the non-hydrazine derivative tranylcypromine (Parnate). In the 1960s and 1970s, the MAOIs were commonly combined with neuroleptic agents. Once such combination was a drug known as Parstelin, a combination of trifluoperazine (Stelazine) and tranylcypromine (Parnate). Now, such combination drugs are no longer used.

MAOIs have continued to be prescribed albeit in markedly decreasing frequency as their use has been dramatically influenced by safety concerns about the tyramine reaction and hypertensive crisis (see below) as well as the fact that they are not promoted by any major pharmaceutical company. Moreover, residents are not exposed to the use of MAOIs during training.

2 Pharmacology of MAOIs, Including Irreversible and Reversible MAOIs

MAO catalyzes the oxidative deamination of monoamines. In humans there are two types of MAO: MAO-A and MAO-B [3]. Serotonin, melatonin, noradrenaline, and adrenaline are primarily deaminated by MAO-A while phenethylamine and benzylamine are deaminated by MAO-B. Both forms break down dopamine, tyramine, and tryptamine equally [4]. Distribution of MAO-A and B varies throughout the body. In most peripheral tissues, MAO isozyme activity is predominately MAO-A [5–7], whereas, in brain MAO-B activity predominates [8].

MAOIs inhibit the deamination or metabolism of the neurotransmitters. The early MAOIs inhibited MAO irreversibly. When they interact with MAO, they permanently deactivate it, and the enzyme function is not restored until the enzyme is replaced. Newer MAOIs, such as moclobemide, are reversible, meaning that when the inhibitor dissociates from the enzyme, activity is restored.

MAOIs are also defined by their selectivity. Some inhibitors selectivity inhibit isozyme A (moclobemide), others selectively inhibit MAO-B (pargyline and selegiline) and some are non-selective (phenelzine, tranylcypromine), inhibiting both A and B. However, selectivity is often concentration dependent and selegiline is truly only selective at low doses, but is non-selective at high doses or concentrations [9].

3 Tyramine Reaction and Hypertensive Crisis

Administration of tyramine results in the displacement of noradrenaline from neuronal storage vesicles. This produces vasoconstriction and an increased heart rate and blood pressure. A tyramine pressor response, which is defined as an increase in systolic blood pressure of 30 mmHg or more, varies between MAOIs and the route of administration (intravenous (IV) vs. oral). Bieck [10] demonstrated that the sensitivity to tyramine was always larger after oral tyramine relative to IV and increased with increasing doses of phenelzine. Compared to the control treatment, blood pressure sensitivity to IV tyramine increased 2.6-fold during phenelzine (60 mg/day), whereas sensitivity to oral tyramine increased from fourfold following 30 mg/day of phenelzine to 15.7-fold following 60 mg/day of phenelzine. This is due largely to an increase in tyramine bioavailability because of MAO-A inhibition in both the liver and intestine.

Non-selective MAOIs generally elicit a greater tyramine pressor response than selective MAOIs. While the peripheral distribution of MAO enzyme would suggest a greater blood pressure response from MAO B inhibition, dose response can confound this interpretation. Nevertheless, Tiller et al. [11] have demonstrated a doubling of the sensitivity (equivalent pressor response with half the tyramine dose) with moclobemide, a selective MAO-A inhibitor. This can be compared to the work of Sunderland [12] who demonstrated a 3.7-fold increase in sensitivity with a 10 mg per day dose of selegiline which was enhanced to a 22-fold increase at 60 mg/day. This is similar to the sensitivity observed with the non-selective tranylcypromine and serves to demonstrate that the selective nature of MAO-B inhibition of selegiline is lost at higher doses [12].

4 Drug Interactions with MAOIs

While many drug–drug interactions occur through inhibition of cytochrome P450, the most serious interactions with MAOIs occur through pharmacologic mechanisms related to the inhibition of MAO. Since serotonin is primarily deaminated by MAO-A, any drug that works as a serotonin reuptake inhibitor (SRI) can produce serotonin syndrome, a dangerous and potentially fatal interaction when combined with an MAOI. SRIs including sertraline, fluoxetine, paroxetine, fluvoxamine, citalopram, escitalopram, TCAs such as clomipramine or imipramine as well as serotonin—noradrenaline reuptake inhibitors (SNRIs) like venlafaxine and duloxetine can produce excessive intra-synaptic serotonin when co-administered with a MAOI [13]. This dual mechanism of inhibition (inhibition of serotonin metabolism and inhibition of reuptake) can lead to clonus, hyperreflexia, hyperthermia and agitation. The onset of toxicity is usually rapid and begins when the second drug is absorbed and reaches effective concentrations. Symptoms subside when one of the drugs has been eliminated. For the SRI or a reversible MAOI this will take about 5 half-lives of the drug. For most drugs this will be <2 weeks [14]. However, for fluoxetine, since the metabolite, norfluoxetine has a half-life of at least 2 weeks [15], the washout period should be much longer.

Some opioid analgesics such as meperidine, tramadol, methadone and dextromethorphan appear to be weak SRIs and have all been reported to cause serotonin syndrome with MAOIs [13]. Even the selective MAO-B inhibitor, selegiline has been reported to cause serotonin syndrome [16]. While this has been reported in a patient receiving only 5-mg of selegiline twice per day [16], pharmacology would predict that this is more likely to occur when the selective nature of selegiline is lost at higher doses.

MAOIs, interaction with indirect acting sympathomimetic amines is perhaps the most likely to occur because of the prevalence of pseudoephedrine and phenylephrine in 'over-the-counter (OTC)' cough and cold—decongestant products. Pseudoephedrine and phenylephrine displace or release adrenaline from the presynaptic nerve. This results in an increase in blood pressure, reported to more than double the pressure response of phenylephrine alone when combined with phenelzine or tranylcypromine [17]. Pseudoephedrine has been replaced with phenylephrine in many decongestant products in North America. However, since both are equally capable of increasing blood pressure, patients should be advised to avoid both pseudoephedrine and phenylephrine containing decongestant products. The commonest nasal decongestant which is not an indirect sympathomimetic amine is oxymetazoline. This adrenergic alpha 2 agonist can be used safely with MAOIs [18].

5 MAOI Diets

Since 1911, it has been known that tyramine which is derived from the amino acid tyrosine, (meaning cheese in Greek) had the potential to increase blood pressure. However, it was in the 1960s when Barry Blackwell [19] published a series of case reports in which hypertensive crises were precipitated by the ingestion of cheese with MAOIs. This alarming discovery at a time of increased "medical legal sensitivity" led to a dramatic decline in the use of MAOIs and also to the development of over inclusive dietary restrictions. In an international survey by Sullivan and Shulman [20] as many as 70 different food items were listed on a variety of MAOI diets.

Over the last 2 decades, Shulman and colleagues [21] conducted a series of careful tyramine analyses in conjunction with a thorough review of case reports and produced a much simpler MAOI diet (see the Appendix, which outlines the Sunnybrook MAOI diet). This diet is an attempt to balance patient compliance with safety concerns and in our experience has proven to be useful and practical. This diet restricts only a very few significant food items including aged cheeses, aged meats, concentrated yeast extracts (marmite), draft beer, sauerkraut, and soy sauces.

6 Irreversible MAOIs

6.1 Efficacy and Effectiveness

Krishnan [22] has reviewed the evidence for the efficacy and effectiveness of irreversible MAOIs for a variety of mood conditions. Overall, studies have shown that in an outpatient population suffering from depression, those treated with MAOIs had a response rate between 50 and 70 %, similar to that of TCA. The three most commonly used MAOIs namely tranylcypromine, phenelzine and isocarboxazid were found to be equally effective in treating major depression [23]. Georgotas et al. [24], found that elderly patients with depression treated with phenelzine did significantly better in terms of recurrence of mood disorder compared to those elderly patients treated with the TCA nortriptyline or compared to placebo. This effect may be related to the increase in MAO observed in older adults [25] and in major depression [26].

Atypical depression is defined by mood reactivity as well as at least two of the following symptoms: hyperphagia or weight gain, increased sleep, subjective feeling of leaden paralysis, and rejection hypersensitivity [27, 28]. It has been estimated that some 30 % of depressives may meet these criteria [29]. In this subtype of depression,

phenelzine was found to be superior to the TCA amitriptyline. Henkel et al. [30], using meta-analysis found a mean effect size of 0.45 favouring MAOIs over placebo and also found a more modest effect size favouring MAOIs over TCAs. In a double-blind randomized controlled trial of phenelzine, imipramine, and placebo, phenelzine, with a response rate of 71 %, was clearly superior to placebo (28 %) and was also significantly better than imipramine with a response rate of 50 % [27].

In studies of TCA resistant patients, approximately 50 % responded to MAOIs [31, 32]. This response rate compared to TCAs was even more pronounced in atypical depression. Krishnan [22] concluded that MAOIs are probably the treatment of choice for later staged treatment resistant depression and may be preferentially helpful with specific subtypes of depression including atypical depression, anergic bipolar depression and anxious/phobic associated depression. In a recent prospective study of treatment resistant unipolar depressed patients discharged from a tertiary unit in the UK, Fekadu et al. [33] found a positive association between treatment with an MAOI and remission at discharge as well as remission at final outcome. They call for renewed attention to the potential role of MAOIs in this especially vulnerable sub-population of mood disorder patients. To further emphasize the potential role of MAOIs in refractory depression, a recent letter from Hamani et al. [34], reports on a patient who had an incomplete response to the experimental treatment of deep brain stimulation. When the tranylcypromine was added at a dose of 40 mg b.i.d., the patient's depression rating score declined sharply from a pretreatment Hamilton Depression Rating Scale score of 22 to only 9 after 4 months. The case report requires further replication, but is yet another example of the potential role of MAOIs in severely ill refractory depressed patients.

MAOIs continue to be listed as second or third line options for treatment resistant depression, atypical depression or bipolar depression in most of the major consensus guidelines including the American Psychiatric Association [35] and the Canadian Network for Mood and Anxiety Treatments (CANMAT) [36]. The American Psychiatric Association, CANMAT, the Texas Algorithm Project [37], and the British Association for Psychopharmacology [38] also recommend MAOIs for treatment of bipolar depression. Despite the significant safety concerns including tyramine and drug interactions, and the lack of industry promotion, irreversible MAOIs continue to be a treatment recommendation by expert clinicians for treatment resistant depression, atypical depression and bipolar depression. A Dutch algorithm for pharmacological treatment of depression includes the use of 'MAOIs as a step four of five steps, just ahead of electroconvulsive therapy [39].

Nolen et al. [40] reported a failed trial of lamotrigine vs tranylcypromine in the treatment of refractory bipolar depression and highlighted some of the methodological challenges in recruiting patients to such a trial. They still concluded that there was a role for tranylcypromine in the treatment of refractory bipolar depression.

Stewart [41] reviewed the treatment of atypical depression and concluded in his analysis that despite some methodological concerns, efficacy reports seemed to favour MAOIs followed by TCAs.

In the STAR*D trial [42], MAOIs were used as a level four treatment in refractory depression [43]. Not surprisingly, in the context of the poor overall results of the STAR*D trial, the effectiveness of the MAOIs was very modest indeed. Treatment with a MAOI yielded a remission rate of 6.9 % and a response rate of 12.1 % in those who had not achieved remission in three prior trials of medication. However, methodological challenges make it difficult to interpret this finding. The average dose of tranylcypromine was low at 36.9 mg/day and maximum dose was 60 mg. Nolen et al. [44] note that most trials of refractory depression used dosages of tranylcypromine up to 100 mg or even higher.

6.2 Safety and Prescription Patterns

A population-based cohort study of older adults on traditional MAOIs utilizing large administrative healthcare databases in Ontario, Canada [45] examined prescription patterns and safety issues. In a ten-year period, only 348 new continuous users of traditional MAOIs were identified in a population of 1.4 million older adults in Ontario. Yearly incidence rates of MAOI prescriptions decreased from 3.1/100,000 in 1997 to 1.4/100,000 in 2006. This occurred during a period of time when antidepressants overall were being prescribed at an increasing rate (10,900/100,000 population) in older adults compared to MAOIs where the prescription rate was only 21.3/100,000 older adults. Not surprisingly, the MAOIs were being used for older adults who had a high prior rate of use of other antidepressants as well as ECT thus confirming its role in refractory depression. In this study, safety concerns were addressed and despite a significant rate of concomitant exposure to at least one serotonin drug (18.1 %) with MAOIs, no case of hypertensive crisis or serotonin syndrome was identified in this database.

7 Second Generation MAOIs

7.1 History

In an attempt to capitalize on the perceived efficacy of traditional irreversible MAOIs for atypical and treatment refractory depression, drug development began to focus on selective and reversible MAOIs, in order to improve safety and convenience. Because hypertensive crises are caused by the inhibition of MAO-A in the gut, selective inhibitors of MAO-B were developed. Selegiline is a selective MAO-B inhibitor at low doses, but it was eventually determined that it was only at higher doses, when selegiline inhibits both MAO-A and MAO-B, that it possessed antidepressant benefits. The next drugs developed were the selective reversible inhibitors of MAO-A. Because these drugs do not bind irreversibly to the MAO in the gut, tyramine is able to displace these drugs, dramatically decreasing its ability to raise blood pressure. The reversible MAO-A inhibitors brofaromine and moclobemide were developed, but only the latter was eventually marketed [46].

More recently development took another approach to avoid the potential for hypertensive crises. Transdermal drug delivery systems avoid first pass metabolism and result in inhibition of MAO in the brain while minimizing MAO inhibition in the gut. Transdermal selegiline was approved by the FDA in 2006, and at low doses (6 mg/24 h) can be administered without dietary restrictions [47].

In spite of improved safety and fewer dietary restrictions, the use of moclobemide and transdermal selegiline never reached the popularity of drugs like the SRIs or SNRIs. While this may be due to concerns about poor efficacy (see below) it is also likely due to their place in clinical practice guidelines. For example, in the American Psychiatric Association Practice Guidelines for major depression [35], MAOIs are not recommended as first line agents but traditional MAOIs or the transdermal selegiline can be considered options for patients who have not responded to SRIs (moclobemide is not available in the US). Other guidelines also omit MAOIs as first line agents and designate them as being for use by specialists only, and frequently never distinguish between traditional MAOIs and moclobemide or transdermal selegiline [48–50]. One of the few guidelines to include moclobemide as a first line antidepressant is CANMAT [36]. In these guidelines, selegiline transdermal is mentioned as a second line agent even though it has not been approved by Canadian Health Regulatory agencies nor is it marketed in Canada.

7.2 Efficacy and Safety of Moclobemide

Numerous meta-analyses have documented the efficacy and safety of moclobemide compared to placebo and other antidepressants. For example, in a meta-analysis by Lotufo-Neto et al. [51], 66 studies of moclobemide published between 1984 and 1996 were included. The response rate of moclobemide was 58 % and no different compared to other antidepressants including TCAs and SRIs. The response rate of moclobemide in studies with placebo was 49 %, and favoured moclobemide significantly by 15.8 %, though the authors noted that the drug-placebo difference was somewhat smaller compared to similar studies with irreversible MAOIs. When they compared moclobemide to individual antidepressants, they found no significant differences with response rates compared to SRIs and TCAs, but lower rates compared to four studies with irreversible MAOIs. In terms of safety, the most common adverse event was insomnia followed by GI disturbances, and only one hypertensive crisis was documented. The authors concluded that moclobemide was as effective as SRIs, and safer and better tolerated than irreversible MAOIs and TCAs, with the clear advantage of having fewer sexual adverse events compared to other antidepressants. Interestingly, the authors also noted the "clinical impression" of MDs in Mexico, Canada, Brazil, the UK, and Europe that moclobemide was not as effective as the irreversible MAOIs. Other meta-analyses found similar results including analyses that focused on studies comparing moclobemide, a relatively activating antidepressant, to more sedating antidepressants for the treatment of agitated, anxious depression [52]. A meta-analysis of MAOIs compared to other antidepressants for the treatment of atypical depression found only two studies with moclobemide [30]. A small study ($N = 53$) of moclobemide compared to fluoxetine found a slight advantage for moclobemide [53], while a larger study comparing moclobemide to sertraline ($N = 172$) found better efficacy for sertraline [54]. These authors concluded that more studies of patients with atypical depression using moclobemide are necessary. Finally, while more studies are clearly required, there is some evidence that moclobemide might be effective for dysthymia [55], and may not be as effective as TCAs for elderly depressives [56].

7.3 Efficacy and Safety of Transdermal Selegiline

Unlike the large number of studies examining the efficacy and safety of moclobemide, there are only four published randomized controlled trials of transdermal selegiline. The first published study included 177 out-patients with a fixed dose of selegiline compared to placebo in which selegiline resulted in statistically significant benefits after six weeks on all outcome measures [57]. In a larger second study with 365 outpatients, 8 weeks of fixed-dose transdermal selegiline was modestly but statistically significantly better than placebo on the primary outcome measures of depression

[58]. In a third flexible-dose study of 265 patients, transdermal selegiline was again modestly but significantly better than placebo [59]. The fourth study was a 52-week, double-blind, fixed-dose study of relapse prevention in 312 patients [60]. Significantly fewer selegiline patients (16.8 %) relapsed after 52 weeks compared to placebo (30.7 %). Selegiline treated patients in these studies experienced more insomnia and more application site skin reactions but virtually no weight gain or sexual adverse events. Also notable was the fact that there were no hypertensive crises in 2,553 patients treated with transdermal selegiline in spite of the lack of dietary restrictions in most of the drug development trials [47]. Finally, from a clinical standpoint, it is notable that these trials demonstrated very high rates of treatment adherence (84–90%) suggesting excellent patient acceptance [14].

Despite reasonable evidence for the effectiveness of selective and reversible MAOIs in the treatment of major depression they have not replaced irreversible MAOIs in the therapeutic armamentarium for atypical depression or treatment refractory depression.

8 Why Are Irreversible MAOIs Not Used More Often?

Traditional MAOIs are not being used despite continued recommendations by opinion leaders, and the inclusion of MAOIs in a wide range of consensus guidelines and treatment algorithms, especially for atypical depressions and treatment refractory depressions. The recent study by Shulman et al. [45] demonstrates that current use of MAOIs appears to be safe and has not resulted in the feared hypertensive crises or serotonin syndromes. Because there are no major pharmaceutical companies promoting MAOIs and due to their "bad reputation", a whole generation of psychiatrists has virtually no experience or knowledge of MAOI use, thereby depriving a subgroup of seriously ill depressive patients from a potentially useful treatment.

In a recent personal opinion paper, Fawcett [61] a respected psychopharmacology expert speculates about why this has occurred. He notes that because of limited numbers available for clinical trials, guidance for this class of drugs is really dependant on the personal experience of opinion leaders. He emphasizes that in his clinical experience, a number of patients with treatment resistant depression do achieve remission when given a trial of MAOIs. He emphasizes that a full course of treatment should be at least 6 weeks in duration at a maximum tolerated dose. Furthermore, in addressing the safety concerns about MAOIs, he notes that in over 40 years of practice he has observed only one case of hypertension with headache that was induced by a dietary factor but was easily managed on an outpatient basis. In reviewing his personal University practice over a five-year period, with a selection bias towards refractory depressive patients, he identified seven patients who were given a trial of MAOIs. Six of those patients achieved remission. He makes a strong case for maintaining this class of drugs in the therapeutic armamentarium for refractory depressions and thereby not depriving the patients of a potentially useful and even life saving treatment.

9 Conclusion

The number of patients with atypical, treatment resistant or bipolar depression who may potentially benefit from MAOIs is substantial [22] and therefore MAOIs could play a role in a much larger proportion of patients than is currently observed. Moreover, the recent reassuring evidence regarding safety concerns should encourage clinicians to be bolder with the use of this class of drugs including the use of practical and safe dietary recommendations while still being alert to the potential for drug interactions, especially with serotonergic agents and amphetamine-like drugs.

There has been a recent flurry of 'clarion calls' to rally interest in the use of MAOIs reflected by terms such as 'unrequited class of anti-depressants' [62], 'risks, benefits and lore' [14] and 'relics reconsidered' [63]. Indeed, Goldberg and Thase [64] have argued that MAOIs represent a currently available 'secret weapon' that provides triple reuptake inhibition. It is really up to experienced clinicians, the profession and the academic community to maintain within our therapeutic armamentarium, treatments that are not promoted by industry yet require special training and knowledge that should be incorporated into psychiatry education programs. In this way we can maintain a treatment that has the potential to benefit a vulnerable and substantial sub-population of mood disorder patients.

Acknowledgments Dr. Shulman is supported in part by the Lewar Chair in Geriatric Psychiatry. Dr. Shulman, Dr. Herrmann and Dr. Walker have no conflicts of interest to declare.

Appendix

SUNNYBROOK HEALTH SCIENCES CENTRE

Dietary Restrictions for Patients Taking MAOI Medication

You are being treated with a medication called an MAOI (monoamine oxidase inhibitor). Several foods and beverages that contain tyramine should be avoided because they may interact with your MAOI medication. **You must follow the dietary instructions below**, from the day before you start taking the MAOI medication until two weeks after you stop taking it. **Always confirm this diet with your treating physician**.

Foods must be fresh or properly frozen. If you are not sure how a food has been stored, do not eat it.

FOODS TO BE AVOIDED	FOODS ALLOWED
Cheese	
All matured or aged cheese. All casseroles made with these cheeses, e.g., lasagna. Please note: All cheeses are considered matured or aged except those listed opposite.	Fresh cottage cheese, cream cheese, ricotta cheese, and processed cheese slices. All fresh milk products that have been stored properly (e.g., sour cream, yoghurt, ice cream).
Meat, Fish, and Poultry	
Fermented/dry sausage: salami, mortadella, summer sausage, etc. Improperly stored meat, fish, or poultry. Improperly stored pickled herring.	All fresh packaged or processed meat (e.g., chicken loaf, hot dogs), fish, or poultry. Store in refrigerator immediately and eat as soon as possible.
Fruits and Vegetables	
Fava or broad bean pods (not beans)	
Banana peel	Banana pulp All others
Beverages	
All On-Tap beer	Alcohol No more than **two** bottled or canned beers or **two** 4 fl. oz. glasses of red or white wine per day. This applies to non-alcoholic beer also. Please note that red wine may produce headache unrelated to a rise in blood pressure
Miscellaneous	
Marmite concentrated yeast extract	Other yeast extract (e.g., Brewer's yeast)
Sauerkraut	Pizza **without aged cheeses** added
Soy sauce and other soy bean condiments	Soy milk, tofu

This list is provided by Sunnybrook as a guideline to assist patients in their selection of foods that will constitute their diet while on MAOIs. Patients should always seek professional advice on the appropriate diet for their particular circumstances.

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