Beta-phenylethylamine, a small molecule with a large impact

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Abstract

During a screen of bacterial nutrients as inhibitors of Escherichia coli O157:H7 biofilm, the Prub research team made an intriguing observation: among 95 carbon and 95 nitrogen sources tested, β-phenylethylamine (PEA) performed best at reducing bacterial cell counts and biofilm amounts, when supplemented to liquid beef broth medium (Lynnes et al., 2013a). This review article summarizes what is known about PEA.

After introducing the chemistry of the molecule, this study focuses on PEA as a neurotransmitter and then moves on to its role in food processing, before detailing the reduction of bacterial cell counts and biofilm amounts. Comparisons to biogenic amines are presented. Briefly, PEA is a trace amine whose molecular mechanism of action differs from biogenic amines, such as serotonin or dopamine. Especially low or high concentrations of PEA may be associated with specific psychological disorders. For those disorders that are characterized by low PEA levels (e.g. attention deficit hyperactivity disorder), PEA has been suggested as a ‘safe’ alternative to drugs, such as amphetamine or methylphenidate, which are accompanied by many undesirable side effects.

In food, PEA and other biogenic amines can be detected as a result of microbial metabolism. As a consequence, these chemicals can be used as indicators of bacterial contamination. Intriguingly, PEA can be found in chocolate, where it is a result of the thermal processing of the CACAO. As a conclusion of this brief review, we will present our own evidence of PEA as an inhibitor of biofilm formation and cell division through a modulation of gene expression.

Introduction

β-phenylethylamine (PEA) is a small molecule that exhibits an array of intriguing and seemingly unrelated functions. The purpose of this review is to summarize general information about PEA as well as detailing a selection of the functions, namely its role as a neurotransmitter and in food processing. Since PEA is a member of the trace amines which are structural and functional relatives of biogenic amines, we present information on other trace amines and biogenic amines as appropriate. General information about PEA is summarized in Chapter I, including the chemical properties of PEA (1.1), its natural occurrence and biological synthesis (1.2), and its chemical synthesis (1.3). Chapter II describes PEA’s functions as a neurotransmitter in three examples of psychological disorders: hyper attention deficit hyperactivity disorder (2.1), depression (2.2), and schizophrenia (2.3). A comparison of PEA’s action to that of other trace and biogenic amines is provided in this Chapter (Illustration 3). Finally, Chapter III describes the role of PEA in food processing, starting with its occurrence in fermented food and meat as a result of microbial metabolism (3.1), and followed by its occurrence in chocolate as a result of thermal processing (3.2). The article concludes with the recently described use of PEA as a modulator of gene expression to reduce biofilm amounts and bacterial cell counts (3.3).

Review

General Information

1.1 Chemical Properties of PEA

PEA is known under a variety of names including β-phenylethylamine, β-phenethylamine, and phenylethylamine. According to the International Union of Pure and Applied Chemistry (IUPAC), the proper name of PEA is 2-phenylethylamine. Its molecular formula is denoted by C_8H_{11}N.

The general information on and the chemical properties of PEA are summarized in Illustration 1. Briefly, PEA has a molecular weight of 121.17964 g/mol, a high solubility in ddH_2O (Cashin, 1972; Shannon et al., 1982), and a short half-life (Shannon et al., 1982). These chemical characteristics impact PEA’s biological functions. In particular, the lack of a methyl group distinguishes PEA from its structural relative, amphetamine.

1.2 Natural Occurrence and Biological Synthesis of PEA

The occurrence of PEA and its derivatives has previously been reviewed (Bentley, 2006). PEA can be found in many algae (Guven et al., 2010), fungi and
bacteria (Kim et al., 2012) as well as a variety of
different plant species (Smith, 1977). PEA is the
decarboxylation product of phenylalanine (Illustration
2A).

Two proposed mechanisms for amino acid
decarboxylation are a pyridoxal phosphate dependent
reaction and a non-pyridoxal phosphate dependent
reaction. The reactions differ in the starting residue;
the first reaction utilizes a pyridoxal-5-phosphate and
the latter uses a pyruvyl residue. The free amino
acids needed for this decarboxylation may be provided
by bacterial proteolysis (Shalaby, 1996). In several
bacterial species, the decarboxylation is catalyzed by
the enzyme tyrosine decarboxylase, which also
converts tyrosine to another trace amine, tyramine
(Marcobal et al., 2012; Pessione et al., 2009).
Intriguingly, PEA synthesized by fungi and bacteria
can also be found in food products (Onal et al., 2013),
where it serves as an indicator of food quality and
freshness. Such foods include the Korean natto (Kim
et al., 2012) and commercial eggs (Figueiredo et al.,
2013). Another food that contains PEA is chocolate,
where it is not produced by bacteria, but during the
thermal processing of cocoa (Granvogl et al., 2006).
PEA can also be found in members of the family
Leguminosae, which is the second-largest family of
seed plants and is comprised of trees, shrubs, vines,
herbs (such as clover), and vegetables (such as beans
and peas). The various different species found within
this family have been used as food, green manure,
and for medicinal purposes (Sanchez-Blanco et al.,
2012). Smith and coworkers hypothesized that plant
synthesized PEA may serve as a defense mechanism
against insects and foraging animals (Smith, 1977).

PEA has also been found in the brains of humans and
other mammals (Paterson et al., 1990; Phillips et al.,
1978). This is attributed to the high solubility of PEA in
plasma and its ability to cross the blood-brain barrier
(Oldendorf, 1971). Like its α-methylated derivative,
amphetamine, PEA has stimulant effects which lead to
the release of so called biogenic amines, including
dopamine and serotonin (Bailey et al., 1987; Rothman
& Baumann, 2006). Unlike amphetamine, PEA is
rarely found in high concentrations in the human body,
due to its oxidative deamination to phenylacetic acid
by the enzyme B monoamine oxidase (MAO) (Yang
& Neff, 1973). Phenylacetic acid has an effect that is
similar to the activity of the natural endorphins, an
effect that is known as a “runner’s high”.

Due to its impact on the levels of several ‘feel good
hormones’ (see above), PEA has recently gained
popularity as a nutritional supplement that is sold by
numerous health stores to improve mood. Since it also
decreases the amount of water intake, it aids weight
loss efforts (Hoffman et al., 2006). Altogether, PEA
appears to have a number of positive effects on
human health without the risks of its structural
relatives.

1.3 Chemical Synthesis of PEA

Two different pathways that lead to the chemical
synthesis of PEA have been established in the 1940s
and 1950s. First, PEA is produced by reduction of a
nitrile into an amine (Robinson & Snyder, 1955).
Specifically, benzyl cyanide is mixed with the
Raney-Nickel catalyst in a calorimeter bomb. The
formation of secondary amines in this reaction is
reduced by the addition of ammonia. The reaction
occurs at 13.9 Mpa and 130°C under hydrogen. The
cooled down liquid is removed from the catalyst by
filtration. This procedure has a yield of 83 to 87%.

A second, simpler way of producing PEA is to reduce
w-nitrostyrene with lithium aluminum hydride in ether
(NYSTROM & BROWN, 1948) (Illustration 2B). The
experimental procedure that employs the use of
lithium aluminum in reduction reactions follows the
mechanism used in a Grignard synthesis.

w-nitrostyrene is added to the previously prepared
lithium aluminum hydride in ether while stirring. This
results in an alcoholate precipitate, which thickens the
solution, requiring more ether to be added. Finally,
using acid hydrolysis, the metal alcoholate is
decomposed and the product can be isolated and
extracted from the ether.

Recent literature focuses on the biological synthesis of
PEA, rather than the chemical one. 1-phenylethylamine
can be synthesized by Escherichia coli overexpressing
ω-transaminase (Cardenas-Fernandez et al., 2012).
Likewise, the PEA biosynthetic enzyme from
Enterococcus faecium can be expressed in E. coli, which
leads to large amounts of L-phenylalanine and tyrosine
decarboxylase activity (Marcobal et al., 2006).
Intriguingly, PEA can serve as a substrate for the synthesis of other drugs, such as
sulfonamides that are being used as anti-microbials
(Rehman et al., 2012).

II. PEA as a Neurotransmitter

PEA is a member of the so-called trace amines
(reviewed by Premont et al., 2001). The expression
“trace amine” is used to refer to a group of amines that
occur at much lower intra- and extra-cellular
concentrations than the chemically and functionally
related biogenic amines and neurotransmitters
epinephrine, norepinephrine, serotonin, dopamine,
and histamine. The molecular mechanism of the trace
amines involves binding to a novel G protein-coupled
receptor, called TAAR (trace amine-associated receptor) (Borowsky et al., 2001; Bunzow et al., 2001), the most studied of which, TAAR1, can be activated by the drug amphetamine as well (Borowsky et al., 2001). The downstream events that follow the initial interaction of PEA and TAAR1 are not nearly as well understood as the receptors and their various ligands themselves (Zucchi et al., 2006); it is however believed that binding of PEA to TAAR1 results in an alteration of the monoamine transporter functions, which leads to inhibition of the re-uptake of dopamine, serotonin, and norepinephrine (Xie & Miller, 2008). Eventually, this will cause an increased concentration of these neurotransmitters at the synapses. A similar increase in the synaptic concentrations of dopamine can be accomplished by blocking the dopamine transporter directly. Methylphenidate is an example of a class of drugs that can perform this blockage (Gatley et al., 1999).

The chemical properties of the biogenic amines, trace amines, and structurally related drugs are summarized in Illustration 3. Illustration 4 is a graphic representation of the regulatory pathway from the trace amine PEA to the increased concentration of the biogenic amines and neurotransmitters dopamine and serotonin. The effects of the drugs amphetamine and methylphenidate are included. Chapter II summarizes the impact of PEA on three psychological disorders, attention deficit hyperactivity disorder, depression, and schizophrenia.

2.1 Attention deficit hyperactivity disorder

A common disease that an estimated 4-9% of young children suffer from is attention deficit hyperactive disorder (ADHD) (reviewed by Cormier, 2008). ADHD is a chronic childhood disorder, which is characterized by a number of behavioral symptoms, including a small attention span, increased frustration, distractibility, and often depression and anxiety (American Psychiatric Association, 2000). ADHD often is paralleled by co-existing psychiatric disorders and patients can have problems that are attributable to ADHD way into their adulthood (Brassett-Harknett & Butler, 2007). Diagnosis of ADHD has traditionally been done by analysis of the symptoms (American Psychiatric Association, 2000). However, this has led to misdiagnosis and, consequently, overmedication. Having a biomarker, in conjunction with a symptomatic diagnosis, could reduce such misdiagnosis and/or overmedication. PEA was recently described as the first such biomarker for ADHD (Scassellati et al., 2012). Specifically, the urinary output of PEA was lower in a population of children suffering from ADHD, as compared to the healthy control population, an observation that was paralleled by reduced PEA levels in ADHD individuals (Baker et al., 1991; Kusaga, 2002). In a consecutive study (Kusaga et al., 2002), those of the children suffering with ADHD were treated with methylphenidate, also known as Ritalin. Patients whose symptoms improved in response to treatment with methylphenidate had a significantly higher PEA level than patients who did not experience such an improvement in their condition (Kusaga et al., 2002).

While this is encouraging, amphetamine and methylphenidate based drugs demonstrate many undesirable side effects, including mild headaches, nausea, insomnia, and constipation. Overdose, whether accidental or intentional, of any of the amphetamine or methylphenidate drugs has been associated with cardiovascular effects, which were attributed to increased levels of extracellular dopamine, norepinephrine, and serotonin (Spiller et al., 2013). While the connection between stimulant drugs such as a treatment for ADHD and cardiovascular disease at this time still appears controversial (Olson et al., 2012), naturopathic professionals have started to recommend PEA as a treatment for ADHD because of the assumed lack of side- and long-term effects.

2.2 Depression

Depression is a very common, sometimes serious disease that affects a wide range of people. It is currently the second leading cause of disability in 15 to 44 year olds. It is predicted that by the year 2030, depression will be the primary cause of disability (World Health Association, 2008). While depression may be most common in the age group of 15 to 44, it can affect people of all ages and backgrounds. Among the characteristics of depression that were summarized in a review article (Voinov et al., 2013), women are 50% more likely to be affected by depression than men and depression can shorten a person’s life by 25-30 years (Voinov et al., 2013).

Most medication that is currently available is about 80% effective for those suffering from depression (Voinov, 2013). Selective serotonin re-uptake inhibitors (SSRI) are the most popular antidepressant prescribed worldwide (Artigas, 2013). SSRI function by blocking the serotonin transporter and thus inhibiting the re-uptake of serotonin (Gutman & Owens, 2006; Peremans et al., 2006). This will result in an increase of the synaptic concentration of serotonin (see Illustration 4). However, SSRI act very slowly at the beginning of the treatment, while exhibiting a range of side effects upon long term use. These long-term side effects include insulin resistance (Chen et al., 2012), bone density loss (Haney et al., 2007), and some poorly understood effects on the offspring...
of mothers with maternal depression (Olivier et al., 2013). Although scientists question the next step in this research (Artigas, 2013), it is clear that novel approaches to depression treatment must be developed. The study by Xie and Miller (Xie & Miller, 2008), which had shown that PEA altered the serotonin transporter by interacting with TAAR, may point towards a safer alternative to SSRI treatment of depression in the form of PEA.

### 2.3 Schizophrenia

Schizophrenia is a rare mental disorder that could potentially be related to PEA. About 1% of the world's population is affected by schizophrenia, which is characterized by problematic thinking and perception (Rossler et al., 2005). Typically, schizophrenia starts around adolescence and will stay with the patients for the rest of their lives, though life expectancy can be largely reduced due to suicide. An additional complication is community attitude because many people perceive schizophrenic patients as potentially dangerous (Stuart & Arboleda-Florez, 2001).

There are different ideas on how one develops schizophrenia. One hypothesis proposes that dopamine contributes to the development of schizophrenia (Howes & Kapur, 2009). In agreement with this hypothesis, patients suffering from schizophrenia are hyper-sensitive to drugs (e.g., methylphenidate) that block the dopamine receptor (Lieberman et al., 1987). A new perspective is given by the TAAR1 receptor (Illustration 4). TAAR1 activation improves the symptoms that are associated with both schizophrenia and depression (in rodent and primate models), without causing the range of negative effects that result from direct blockage of the dopamine receptor (Revel et al., 2013).

Among other factors that may contribute to schizophrenia are inflammatory cytokines (Zakharyan et al., 2013) and phospholipase (Koh, 2013). Altogether, schizophrenia may be the most complex of the psychological disorders discussed in this study and it is quite apparent that many factors contribute to its development.

### III. PEA and other Amines in Food

PEA is connected to food processing in several, seemingly unrelated ways. First, PEA and other amines can be found in food as a result of the metabolic activity of bacteria (3.1). As a consequence of this, PEA can be used as a biomarker for contamination of food by the respective bacteria. A second process which does not involve bacterial metabolism can lead to the production of PEA in chocolate through the thermal processing of cocoa (3.2). Finally, research by our own lab has shown that PEA can be added to food intentionally to modulate gene expression which will lead to phenotypes that are less harmful to humans. Two such phenotypes are a reduction in biofilm amounts and reduced bacterial cell counts of *E. coli* O157:H7 (3.3).

#### 3.1 PEA and other amines in food as a result of microbial contamination

Some foods that contain microorganisms can release high levels of amines, including the trace amines PEA, tyramine, and tryptamine, the biogenic amine histamine, and the polyamines putrescine and cadaverine (Shalaby, 1996). Such amines are formed by bacteria of the genera *Lactobacillus*, *Clostridium*, *Pseudomonas*, and *Enterobacteriaceae* that contain amino acid decarboxylases, which remove an α-carboxyl group from the respective amino acid (Giraffa, 2003; Shalaby, 1996).

This increased concentration of amines is due to bacterial metabolic processes and is commonly associated with foods and food products made through the process of fermentation (Bunkova et al., 2013). A good example of this is the “cheese reaction”, which refers to high levels of tyramine as a result of elevated levels of tyrosine in cheese that has had increased storage times at temperatures higher than recommended by the producer. As mentioned earlier (Chapter 1.2), PEA can be a by-product of the tyrosine decarboxylase reaction because the same enzyme that is capable of converting tyrosine to tyramine can also metabolize phenylalanine to PEA (Marcobal et al., 2012). In individuals taking monoamine oxidase inhibiting drugs, the ‘cheese reaction’ can result in a hypertensive crisis (Boulton et al., 1970; Da et al., 1988; Deftereos et al., 2012).

A second group of food or food product that contains elevated levels of amines is meat and/or fish (Kulawiak et al., 2013; Li et al., 2012; Liu et al., 2013), where amine production is part of the food spoilage reaction and can be used as an indicator of food freshness and quality. Specifically, bacteria from the families *Enterobacteriaceae* and *Pseudomonadaceae* can produce cadaverine and putrescine in spoiled turkey meat. Fraqueza and coworkers suggested to use tyramine, putrescine, and cadaverin to quantify meat freshness (Fraqueza et al., 2012). In vegetables, high levels of tyramine were only seen in brine, unless the vegetables were contaminated prior to processing or the temperature and storage time were extreme (Moret et al., 2005).

Since elevated levels of amines are usually an indicator of food spoilage, it is possible to use...
detection of amines as an indicator of food freshness. One such technique is thin-layer chromatography to separate and identify amounts of tyramine and PEA (Garcia-Moruno et al., 2005).

3.2 PEA in chocolate as a result of thermal processing

The connection between “food and mood” was recognized long time ago (Ottley, 2000). In particular, chocolate craving has been the focus of intense research (Durkin et al., 2012; Hormes & Timko, 2011; Werthmann et al., 2013). Lately, the combination of chocolate with coffee has been proposed as “a novel elixir for a long and happy life” (Dal Moro, 2013). Besides a number of other beneficial substances (e.g. antioxidants), chocolate also contains trace amounts of PEA (Ziegleder et al., 1992), a result of the thermal processing and fermentation of cocoa (Granvogl et al., 2006). Since we mentioned earlier that PEA is promoted to aid weight loss, one may conclude that if a person eats enough chocolate they will lose weight! Careful readers, please note: in a study that attempted to determine the concentration of PEA in chocolate, the detection limit for PEA was 3 mg/kg of chocolate and the concentration of PEA in their chocolate samples was below this limit (Pastore et al., 2005). In contrast, the recommendation for PEA as a nutritional supplement is currently 500 mg/day (for an example, please, see http://www.bodybuilding warehouse.com). This means that the concentration of PEA in chocolate is not high enough to induce weight loss, so eating chocolate will still lead to weight gain.

One interesting controversy around chocolate and PEA is the question of whether chocolate can cause migraine and whether this may be due to PEA. Of course, food in general can trigger migraine (Finocchi & Sivori, 2012). Also, individual studies point towards chocolate as one of those foods (Fukui et al., 2008), but other studies are in contrast with these findings (Marcus et al., 1997). The fact that other foods that contain PEA, tyramine, or histamine (e.g. cheese and wine) may also trigger migraine (Werthmann et al., 2013) raised the question whether dietary amines may be responsible for this response. This question is justified, considering that PEA causes the release of nor-epinephrine into the synaptic space, which consequently constricts the aorta and the coronary arteries (Broadley et al., 2009). However, results among various studies are inconclusive (Jansen et al., 2003), and the connection between chocolate and migraines remains a mystery.

3.3 PEA as a modulator of bacterial gene expression

In Chapter 3.1, we discussed contamination and food spoilage by bacteria. One such initially contaminated food can cross-contaminate additional food products through the food processing chain because of the bacteria’s ability to attach to food contact surfaces and form biofilm (Giaouris et al., 2013).

Recent research advances that are aimed at the prevention of biofilm include the manipulation of the bacteria’s signal transduction pathways, including quorum sensing (Bassler, 2010) and two-component signaling (Lynnes et al., 2013b). One such environmental signal that bacteria can respond to is PEA, whose signal transduction pathway may include the flagellar and global regulator complex FihD/FihC (Stevenson et al., 2013). A reduction in flagella synthesis would be expected to inhibit the first phase of biofilm formation, reversible attachment. In our own research lab (Lynnes et al., 2013a), PEA was the most inhibitory of the 95 carbon and 95 nitrogen sources screened for their effect on E. coli O157:H7 growth, bacterial cell counts, and biofilm amounts. In liquid beef broth medium, PEA reduced biofilm amounts. Intriguingly, bacterial cell counts were reduced at the same time and with a similar inhibitory concentration. In contrast, the effect of PEA on bacterial growth, as measured by the optical density of the culture, was affected only at a much higher concentration of PEA. In a final experiment, bacterial cell counts of E. coli O157:H7 were determined from beef meat pieces that were treated with different dilutions of PEA and subsequently inoculated with the bacteria; this resulted in a 90% reduction of bacterial cell counts when the beef was treated with a concentration of PEA at 150 mg/ml. We were unable to determine biofilm formation on the beef meat pieces. Altogether, this study demonstrated how PEA could be used to alter gene expression in order to reduce biofilm formation and bacterial cell counts (Lynnes et al., 2013a). The question arises whether it could be possible to integrate PEA into novel biomaterials that can then be used to coat food processing equipment to prevent biofilm formation on such equipment and cross contamination during the food processing chain.

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Authors Contribution(s)

All authors contributed equally to the work.

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chocolate is related to craving and self-endorsed eating permission. Appetite 70C: 81-89.
Illustrations

Illustration 1

Table 1

<table>
<thead>
<tr>
<th></th>
<th>Solvent independent properties</th>
<th>Solvent dependent properties</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>In ddH$_2$O</td>
<td>In lipid</td>
</tr>
<tr>
<td>Molecular weight</td>
<td>121.17964 g/mol</td>
<td>NA</td>
<td>NA</td>
</tr>
<tr>
<td>Companies that sell PEA</td>
<td>Forest Health, Vitacost, Amazon, Walmart</td>
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<td>NA</td>
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<tr>
<td>Toxicity</td>
<td>Mouse LD$_{50}$ (oral) 400 mg/kg</td>
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<td>NA</td>
</tr>
<tr>
<td>Solubility</td>
<td>NA</td>
<td>High solubility</td>
<td>Low solubility</td>
</tr>
<tr>
<td>Half life</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
</tr>
</tbody>
</table>
Illustration 2

Figure

A

\[
\text{A} \quad \text{Acid} \quad \xrightarrow{\text{Esterification}} \quad \text{Alkylamine} + \text{CO}_2
\]

B

\[
\text{B} \quad \text{Nitroalkane} + \text{LiAlH}_4 \quad \xrightarrow{\text{Esterification}} \quad \text{Alkylamine}
\]
### Illustration 3

Properties and functions of biogenic amines, trace amines and structurally related drugs

<table>
<thead>
<tr>
<th>Name</th>
<th>Structure</th>
<th>Synthesized from:</th>
<th>Functions</th>
</tr>
</thead>
</table>
| Dopamine              | ![Dopamine](#) | L-Tyrosine        | CNS: regulates movement  
                        |                        | Blood vessels: vasodilation                                             |
| Serotonin             | ![Serotonin](#) | L-Tryptophan      | CNS: mood, sleep, memory, and learning  
                        |                        | Gut: intestinal movement                                                |
| Histamine             | ![Histamine](#) | Histidine         | CNS: sleep  
                        |                        | Immune system: inflammatory response (allergy)                         |
| Epinephrine (Adrenaline) | ![Epinephrine](#) | Tyrosine via dopamine and nor-epinephrine | CNS: stress response (fight or flight)  
                        |                        | Blood vessels: vasoconstriction                                          |
| Nor-epinephrine (Nor-adrenaline) | ![Nor-epinephrine](#) | Tyrosine via dopamine | CNS: heart contractions (heart rate), vascular tone (blood pressure) |
### II. Trace Amines

<table>
<thead>
<tr>
<th>Name</th>
<th>Structure</th>
<th>Synthesized from:</th>
<th>Protein Targets</th>
</tr>
</thead>
<tbody>
<tr>
<td>β-phenyl-ethylamine (PEA)</td>
<td><img src="C05332" alt="Structure" /></td>
<td>L-Phenylalanine</td>
<td>TAAR1</td>
</tr>
<tr>
<td>p-Tyramine</td>
<td><img src="C00483" alt="Structure" /></td>
<td>L-Tyrosine</td>
<td>TAAR1; dopamine receptor</td>
</tr>
<tr>
<td>Tryptamine</td>
<td><img src="C00390" alt="Structure" /></td>
<td>L-Tryptophan</td>
<td>5-hydroxytryptamine receptor; NFkB1; Cytochrome P450</td>
</tr>
<tr>
<td>Octopamine</td>
<td><img src="C04227" alt="Structure" /></td>
<td>Tyrosine via tyramine</td>
<td>TAAR1</td>
</tr>
</tbody>
</table>

### III. Structurally related Drugs

<table>
<thead>
<tr>
<th>Name</th>
<th>Structure</th>
<th>Synthesized from:</th>
<th>Function</th>
</tr>
</thead>
<tbody>
<tr>
<td>Amphetamine</td>
<td><img src="C07614" alt="Structure" /></td>
<td>Ephedrine</td>
<td>A stimulant of the central nervous system that mimics the effects of dopamine, epinephrine, and norepinephrine.</td>
</tr>
</tbody>
</table>
Methyl-phenidate Piperidine derivative A stimulant of the central nervous system that are used to treat attention deficit disorders and narcolepsy.
Illustration 4

Fig 4

Illustration 3: Schematic of the inhibition of the dopamine and serotonin transporters by PEA, amphetamine, and methylphenidate. Panel A shows the normal action of release and re-uptake of the biogenic amines: dopamine and serotonin. Panel B shows the modulation of the monoamine re-uptake transporters by PEA and amphetamine through TAAR, as well as the blockage of the dopamine transporter by methylphenidate.

Serotonin, dopamine, serotonin receptor, dopamine receptor, PEA, amphetamine, methylphenidate.