International Journal of Advance Research in Science and Engineering
Volume No. 12, Issue No. 05, May 2023
www.ijarse.com
IJARSE
ISSN 2319 - 8354

A MINI REVIEW ON PHARMACOLOGICAL ACTIVITY AND CHEMISTRY OF ANTHRANILIC ACID DERIVATIVES

[1]Madhu Bala , [2]Dr. Veer Singh,[3]Dr. Amit Girdhar

Research Scholar, Ph.D (Chemistry), SKDU, Hanumangarh (Raj.), A.P in Chemistry,
JCD Memorial College, JCD Vidyapeeth, Sirsa,
A.P in Chemistry, Deptt. Of Chemistry, SKDU, Hanumangarh(Raj.)
Professor, JCDM college of Pharmacy, JCD Vidyapeeth, Sirsa

ABSTRACT

Anthranilic acid and N-Phenyl anthranilic acids are serving as precursors for many potent drugs nowadays. The metal complexes of these acids and their derivatives are used in coordination chemistry as their complexes shows higher activity than their ligands. These derivatives are synthesized from various chemical reactions and are also derived from plant and animal resources. Molecular docking is another way to get potent and effective derivatives. Many pharmacological activities such as COX inhibitors, α-glucosidase inhibitors, aldo keto reductase undecaprenyl pyrophosphate synthase (UppS) inhibitors, urease inhibitors, MAPK (mitogen activated protein kinase) and many more are reported till date. These analogs are evaluated for their anti-inflammatory, analgesic, anticancer, antidiabetic, antiviral, antimicrobial and various other properties by different screening methods and bio evaluation. The present review demonstrates a critical analysis on pharmacological properties of several anthranilic acid based pharmaceuticals.

INTRODUCTION

Anthranilic acid (2-aminobenzoic acid, AA) is a versatile and low cost starting material for synthesis of benzofused heterocycles. (Wiklund & Bergman, 2006). Anthranilic acid and its derivatives present a privileged profile as pharmacophores for the rational development of pharmaceuticals deliberated for managing the pathophysiology and pathogenesis of various diseases. (Prasher & Sharma, 2021). These derivatives are considered a cheap and efficient stating precursor for the production and synthesis of various marketed available drugs like furosemide (diuretic), tranilast (antiallergic), betrixaban (anticoagulant) and analgesic & anti-inflammatory fenamates. Numerous anthranilic acid analogs with potential anticancer, antimicrobial, insecticidal, antiviral, anti-inflammatory activities and other biological activities have been disclosed over the last thirty years. (Nasr et al., 2022). The research history includes n-phenyl anthranilic acid as an agent for inducing and studying renal papillary necrosis in the rat.(Hardy, 1970) and pharmacological properties of n-(3',4'dimethoxycinnamoyl) anthranilic acid (n-5'), a new anti-atopic agent. (Azuma et al., 1976). From these initial results we have reached to an era where these precursors and derivatives have shown potent anticancer, anti-diabetic and antiviral properties.The anthranilic acid and its analogues have functional head groups,

including COOH, NH2, CONH2, COOCH3, and NHCOCH3, which allow for their conjugation and derivatization to create carefully thought-out molecules that are intended to interact with their biological targets (Kwon et al., 2017; Schrey et al., 2019; Teponno et al., 2017). These functional groups serve as places for tailoring molecules, analysing the structure-activity relationship (SAR) analyses of anthranilic acid-based libraries, for the screening of potent molecules.

CLASSIFICATION OF ANTHRANILIC ACID ANALOGUES ON BASIS OF THEIR PHARMACOLOGICAL ACTIVITIES:

A. Derivatives showing anti-Inflammatory activity

B. Derivatives showing antimicrobial activity

C. Derivatives showing antidiabetic activity

D. Derivatives showing anticancer activity

E. Derivatives for treatment of Schizophrenia

A. ANTI-INFLAMMATORY COMPOUNDS

A.1 Derivatives of anthranilic sulfonamides that inhibit COX-2 enzyme

Fenamates, a significant class of anti-inflammatory medications, include anthranilates. The COX-2 enzyme, an inducible isoform of the cyclooxygenase family of enzymes, is selectively inhibited by members of the fenamates class (Prasher et al., 2019; Singh et al., 2015). The purposeful compounds' presence of a bulky group, which enables quick entry and optimal accommodation of the drug molecule to the active site loop of COX-2 enzyme, is primarily responsible for the selective suppression of the COX-2 isoform (Prasher et al., 2021). Contrarily, the COX-1 enzyme's smaller substrate entry site prevents drugs from reaching its active site (Ferrer et al., 2019). N-sulfonyl anthranilic acid derivatives were created by (Han et al., 2017) as anti-inflammatory drugs that bind to the COX-2 active site directly. These compounds' larger sulfonyl groups enabled these compounds to bind to and inhibit the COX-2 isoform specifically.

A.4 Derivatives for treatment of Rheumatoid Arthritis

The findings of (Morsy et al., 2022) demonstrate the efficacy and security of two recently discovered anthranilic acid derivatives as anti-inflammatory drugs in a well-established RA model. The outcomes also show that, despite the latter's better COX-2 selectivity, have equivalent anti-inflammatory effects. Additionally, the derivatives showed enhanced safety profiles and slightly more potent anti-inflammatory effects than regular mefenamic acid, particularly at the level of cytokine expression.

A.3 Anthranilic diamide-based anti-ulcerogenic analgesics

The main adverse impact of conventional anti-inflammatory therapy is mucosal layer erosion, which is caused by the representative NSAIDs and analgesics (Rayado et al., 2018; Takeuchi & Amagase, 2018). Fenamates isosteres were shown to have anti-ulcerogenic effects in addition to a strong anti-inflammatory potential by

(Alafeefy et al., 2015). Acute toxicity on the test substances led to a negligible degeneration in liver tissues and trivial necrosis in hepatocytes, further validating their biological tolerance. These test compounds, as opposed to the representative NSAIDs, generated few side effects, provided the best anti-inflammatory activities, and had improved gastrointestinal tolerance.

A.4 Nphenyl anthranilic amide-based anti-inflammatory drugs

The amide derivatives of maclofenamic acid with an increased antiinflammatory action were described by (Narsinghani and Sharma, 2017). According to in vitro enzyme immunoassays and in vivo tests on animal models, the test compounds specifically suppressed the inducible COX-2 isoenzyme. The significant hydrogen bonding interactions that were shown by the test compounds' docking study in the active site of the COX-1 isoenzyme further support the use of these substances as anti-inflammatory drugs.

B. ANTIMICROBIAL COMPOUNDS

B.1 NS5B polymerase inhibitors for the hepatitis C virus based on anthranilic acid

By specifically focusing on the viral proteins required for HCV replication, direct acting molecular inhibitors have a notable impact on the therapeutic paradigm for hepatitis C virus (HCV) (Boyce et al., 2014). In order to replicate viral RNA, the viral protein NS5B functions as an RNA-dependent RNA-polymerase, which uses the viral positive RNA strand as a template (Wei et al., 2016). Compounds were created as a result of deliberate attempts to create the Thumb Pocket 2 HCV NS5B polymerase inhibitors, and they are based on the pharmacophore anthranilic sulfonamide. SAR study showed that the major pharmacophore was improved by adding an ortho-trifluoromethyl group and replacing the arylsulfonamide group with trans-4-methylcyclohexyl-N-iPr carboxamide substituent. According to (Stammers et al., 2013), the test derivative with a 5-(ortho-trifluoromethyl) phenoxy substitution on the anthranilic acid moiety interacted favourably with the shallow lipophilic pocket located on the binding site of HCV NS5B polymerase. Notably, the addition of the nonaromatic substituent "cyclopentoxyl" provided a significant level of HCV NS5B polymerase inhibitory potency. A thorough in silico study using molecular docking and 3D-QSAR for virtually screening the potential hits and leads was motivated by the favourable effects of anthranilic diarylamines in limiting the reproduction of the Zika virus (Silva et al., 2019).

B.2 Antimicrobial substances that target UppS based on anthranilic acid

The enzyme undecaprenyl pyrophosphate synthase (UppS), which catalyses the condensation of farnesyl pyrophosphate with isopentenyl pyrophosphate units, is essential for the formation of the bacterial cell wall. It is a desirable target in the development of antibacterial drugs since it also functions as a lipid carrier for the manufacture of peptidoglycans (Egan et al., 2020; Workman et al., 2018; Workman & Strynadka, 2020). In order to prevent the formation of the bacterial cell wall, (Jukic et al., 2019) described the rationally created inhibitors of UppS. The new anthranilamide analogues successfully mirrored the structure of the polar pyrophosphate group and lipophilic moieties found in the UppS substrates farnesyl pyrophosphate (FPP) and isopentenyl pyrophosphate (IPP), which is significant.

B.3 Anthranilic diamide-based antiviral substances

The trifluoromethyl pyridine and hydrazone moieties that were rationally designed anthranilic diamide derivatives were appended with presented antiviral activities against the tobacco mosaic virus and cucumber mosaic virus in plants. Comparing the test compounds to ningnanmycin and ribavirin, a significant curative effect was provided. According to (Wang et al., 2019), the test compounds showed strong binding affinity towards the viral coat proteins and hindered the self-assembly of virus particles. The virus's coat protein safeguards its nucleic acid, aids in infection or transmission, is essential for mRNA transcription and translation, and promotes the self-assembly of virus particles. As a result, these vital processes required for the virus' survival were blocked by the test variants' binding to the coat proteins (Sharma et al., 2020).

C. ANTIDIABETIC COMPOUNDS

C.1 Anthranilic acid-based metal complex-based -glucosidases inhibitors

During the intestinal digestion of carbohydrates and a number of important metabolic processes, including the catabolism of lysosomal glycoconjugates and oligosaccharide production, -glucosidases mediate the processing of glycolipids and glycoproteins. In the treatment of obesity, diabetes mellitus, metastatic malignancies, and immunodeficiency virus infections, the modulation of -glucosidases activity by rationally designed drugs has been shown to be therapeutically effective (Hedrington & Davis, 2019). The metal complexes of the anthranilic acid derivatives were described by (Zheng and Ma., 2016) as a novel family of non-competitive inhibitors of -glucosidase. The in vitro research revealed that the ligand complexes had a better biological profile than free ligands and metal ions. With a 4000-fold greater activity than the free ligands, the ligand complexes with Ag (I) showed the most notable inhibition of -glucosidase.

C.3 α-Glucosidases inhibitors based on anthranilic diamide

The anthranilic diamide pharmacophore based rationally developed compounds demonstrated dual inhibition of -glucosidase and Glycogen phosphorylase for the achievement of the antidiabetic actions. The N-pyridyl nucleus-containing test compounds demonstrated strong anti-diabetic effects by dramatically decreasing the abnormal blood glucose level. The test compounds' anti-diabetic activity was further confirmed by the molecular docking analysis of their interactions with the target enzymes' active site residues (Ihmaid, 2018).

D. ANTICANCER COMPOUNDS

D.1 Aldo-keto reductase enzyme inhibitors

The collaboration between the several regulatory pathways that operate in tandem to display the oncologic pathogenesis is incorporated into the pathophysiology of cancer (Prasher et al., 2021). Aldo-keto reductase enzymes (AKR1C1 through AKR1C4) are members of the family of hydroxysteroid dehydrogenases and catalyse NADP(H)-mediated reductions during biosynthesis, detoxification, and intermediate metabolism (Zheng et al., 2017). These enzymes are allegedly involved in malignant transformations and are crucial in maintaining cancer cells' resistance to chemotherapy (Matsunaga et al., 2013). Because AKR1C3 plays a role in the generation of androgen in prostate cancers, there are now molecular inhibitors of AKR1C3 based on the pharmacophore N-phenyl anthranilic acid. The results of the SAR analysis of the described compounds revealed

that the phenylamino ring's electron-withdrawing substituents presented an optimal inhibition of AKR1C3. The positioning of the rationally designed compounds in the AKR1C3 enzyme's active site suggested hydrogen bonding interactions between the free COOH group on one ring and the NH group connecting the two phenyl rings. The latter's interaction with the carboxamide group of the NADP (H) cofactor enables the anchoring of the test compounds to the enzyme active site. Higher selectivity for AKR1C3 was imparted to the test compounds by the presence of larger and polar substituents on the phenylamino ring as a result of improved interactions with the unique SP1 subpocket of the target enzyme. Similar to this, the pKa values of the NH and COOH groups are disturbed by the phenylamino ring substituents that changed the aromatic framework's electron density. It affected the test chemicals' ability to create hydrogen bonds in the target enzyme's active region, thereby reducing their activity. Comparing the test compounds to the commercial inhibitor abiraterone acetate, which is frequently supplied along with glucocorticoids, it appears that the test compounds showed a higher inhibitory profile towards AKR1C3. The direct inhibition of AKR1C3, which acts downstream in the androgen biosynthesis pathway, serves as a more effective method in the management of prostate cancer because long-term usage of glucocorticoids induces immunosuppression and Cushing's syndrome (Adeniji et al., 2021).

The N-phenyl anthranilic acid pharmacophore, which filled the specific SP1 pocket of the target enzyme, and the test compounds, had varied interactions with the active site residues. According to (Sinreih et al., 2012), the test compounds demonstrated a selective inhibition of the AKR1C3 enzyme and offered a strong case for the treatment of hormone-dependent and -independent breast and prostate cancers.

D.2 Hedgehog signalling pathway inhibitors

In embryogenesis, tissue homeostasis, smooth muscle differentiation, and cell proliferation, the hedgehog signalling pathway represents a conserved signalling mechanism (Iriana et al., 2021; Jeng et al., 2020; Quaglio et al., 2020). The activity of the proteins connected to the hedgehog pathway is regulated by posttranslational modifications, different transcriptional processes, and nuclear cytoplasmic shuttling (Sari et al., 2018). In addition to generating basal cell carcinoma, the abnormal activation and overexpression of the hedgehog pathway is implicated in the development of solid tumours by the conversion of adult stem cells into cancer stem cells. The anthranilamide derivatives were developed by (Ji et al., 2020) as potent inhibitors of the hedgehog pathway that exhibited anti-proliferative activities against Daoy cells. The dual luciferase-reporter gene assay's calculation of the test compounds' IC50 revealed the importance of the electronic effects of different substituents on the phenyl ring on the activity of the test compounds. The human smoothened 7TM receptor, a downstream protein in the hedgehog signalling system, participates in stacking interactions with the active site residues of the phenyl ring having 2-trifluoromethyl-4-fluoro substituent. According to molecular docking studies, compounds that successfully form hydrogen-bonding interactions with the downstream protein's active site residues in the hedgehog pathway showed improved accommodation in the active site loop and higher inhibitory potential. The NH and CO groups in the anthranilamide moiety caused the hydrogen bonding interactions to manifest.

D.3 Agents that induce apoptosis

The pathophysiology of cancer is manifested by the dysregulation of apoptosis, which is the damaged cells' planned cell death. Modern anticancer therapy relies heavily on targeting the intact apoptotic signalling pathways (Pistritto et al., 2016). Using novel techniques, (Liu et al., 2013) produced anthranilamide and anthranilic diamide. The apoptosis inducers in derivatives were used to achieve the anticancer activity. The proliferation of HCT 116, MDA-MB-231, and VEGFR-2 cells was apparently inhibited by the test chemicals' dose-dependent induction of apoptosis, which arrested the G1 and S phases of the cell cycle. The test compounds that had adaptable linkers between the anthranilamide's amino group and aromatic ring primarily shown a positive anti proliferative activity in the test cell lines. Similar to this, the electronic withdrawing substituents on the benzene ring in the test compounds showed a considerable suppression of cell proliferation that achieved an apoptotic impact in the test cell lines.

D.4 Mitogen-activated protein kinase-5 signalling pathway inhibitors

Gene expression, cell proliferation, and survival are all controlled by mitogen activated protein kinase-5 (MAPK-5) signalling pathways. According to Braicu et al. (2019), abnormal MAPK signalling expression leads to uncontrolled cell proliferation and a diminished cellular response to apoptosis. The MAPK pathway is a complicated interconnected signalling cascade with many kinases linked to tumour development and oncogenesis (Lee et al., 2020). Extracellular signal-regulated kinase (ERK) is a component of the highly branched MAPK signalling cascade and is phosphorylated by the MEK that it is paired with (MAPK/ERK kinases). N-phenyl anthranilic acid derivatives' impact on MAPK-5 signalling pathways was investigated by Chakrabarty et al. (2018). The MEK/ERK signalling cascades that the test derivatives interacted with were successful in treating tumours.

According to the SAR analysis of the test compounds, the inclusion of the piperazine substituent showed a high efficacy and distinct selectivity for inhibiting the MEK5/ERK5 cascade. Similar to this, selectivity against ERK1/2 cascades was achieved by the presence of basic, substituted amino substituents. When compared to the halogen bonding from terminal arenes, the positioning of cationic amine substituents in an ideal orientation because of the internal hydrogen bonding was more advantageous. Notably, the MEK5 selectivity in rotationally constrained compounds with cationic side chains was greatly influenced by the presence of the 4-iodine substituent. Similarly, MEK5 selectivity was favoured by the presence of free rotating N,N-diphenylaniline carboxylates. The most active molecule, 25 mg/kg, caused a considerable decrease in tumour volume in animal models, proving that the test compounds simultaneously inhibited the MEK1/2 and MEK5 cascades.

D.5 Derivatives with cytotoxic properties

By modifying the anthranilic acid nucleus with the appropriate substituents, bioactive molecules with pronounced cytotoxicity against cancer cell lines are produced. These substances had antitumor activities and made a strong case for being developed into the upcoming anticancer medicines. Shi et al. (2012) developed a novel series of compounds based on anthranilic diamide pharmacophore containing arylisoxazoline nucleus 35 a-o (Figure 7) with cytotoxic properties and antitumor potency against human lung cancer (NCI-H460), breast epithelial adenocarcinoma (MCF-7), hepatocellular liver carcinoma (HepG2), and gastric cancer (SCG-7901,

BGC-823) cell lines. An extensive SAR analysis of the test compounds revealed that the electronic effects of substituents play a key role in determining the test compounds' anticancer effectiveness. The in vitro research on cancer cell lines demonstrated the test derivatives' anticancer capability.

E. DERIVATIVES FOR TREATMENT OF SCHIZOPHRENIA

The most recent theory about the mechanisms of schizophrenia is the dysregulation of the Trp-Kyn pathway. One of the three immediate downstream metabolites of kynurenine (Kyn), along the tryptophan (Trp):Kyn pathway, kynurenic acid (KYNA), in particular, has been thought of as a new target for therapeutic intervention in schizophrenia. It was proposed that KYNA formation, the second immediate downstream metabolite of Kyn, was up-regulated at the expense of 3-hydroxyKyn (3-HK), whose production was down-regulated. According to (Oxenkrug, 2016) preliminary findings, people with schizophrenia have dramatically and significantly higher serum levels of AA. Though it hasn't been thought of yet, AA may play a role in the mechanisms underlying schizophrenia. A new target for therapeutic intervention in schizophrenia, AA should be further studied as a biological marker of at least a subgroup of schizophrenia patients (e.g., linked to autoimmune mechanisms).

CONCLUSION

The anthranilic acid analogues and their derivatives offer a remarkable therapeutic profile for the design of carefully considered molecules intended to control oncogenic pathways, metabolic complications related to diabetes, cutting-edge antiviral agents, and biologically tolerable anti-inflammatory compounds. Anthranilic acid is a key building block of various pharmacological classes, including fenamates and NSAIDs, and it is used as a precursor in the production of a number of commercial medications and pharmaceuticals. The range of the SAR analysis of the resulting compounds is increased by the covalent anchoring provided by the free COOH and NH2 functions, which can bind to a variety of substituents, linkers, and functional head groups. Many anthranilic acid-based medicines have had clinical success, and their subsequent commercialization proves their eligibility for the production of impending medicinally relevant molecules.

REFERENCES:

1. ***British J Pharmacology—2009—Kraft—Inhibition of TRPM2 cation channels by N-***
2. *p-amylcinnamoyl anthranilic acid.pdf*. (n.d.).
3. **Chakrabarty, S., Monlish, D. A., Gupta, M., Wright, T. D., Hoang, V. T., Fedak, M., Chopra, I., Flaherty, P. T., Madura, J., Mannepelli, S., Burow, M. E., & Cavanaugh, J. E. (2018).** Structure activity relationships of anthranilic acid-based compounds on cellular and in vivo mitogen activated protein kinase-5 signaling pathways. *Bioorganic & Medicinal Chemistry Letters*, *28*(13), 2294–2301. https://doi.org/10.1016/j.bmcl.2018.05.029.
4. **El-Zahabi, H. S. A., Abdulwahab, H. G., Edrees, M. M., & Hegab, A. M. (2019).** Utility of anthranilic acid and diethylacetylenedicarboxylate for the synthesis of nitrogenous organo/organometallic compounds as urease inhibitors. *Archiv Der Pharmazie*, *352*(7), 1800314. https://doi.org/10.1002/ardp.201800314.
5. **Faïon, L., Djaout, K., Pintiala, C., Piveteau, C., Leroux, F., Biela, A., Slupek, S., Antoine, R., Záhorszká, M., Cantrelle, F.-X., Hanoulle, X., Korduláková, J., Deprez, B., Willand, N., Baulard, A. R., & Flipo, M.**

(2023). Exploring the Antitubercular Activity of Anthranilic Acid Derivatives: From MabA (FabG1) Inhibition to Intrabacterial Acidification. *Pharmaceuticals*, *16*(3), 335. https://doi.org/10.3390/ph16030335.

6. **Han, S. H., Suh, H. S., Jo, H., Oh, Y., Mishra, N. K., Han, S., Kim, H. S., Jung, Y. H., Lee, B. M., & Kim, I. S. (2017).** Synthesis and anti-inflammatory evaluation of N -sulfonyl anthranilic acids via Ir(III)-catalyzed C–H amidation of benzoic acids. *Bioorganic & Medicinal Chemistry Letters*, *27*(10), 2129–2134. https://doi.org/10.1016/j.bmcl.2017.03.072.
7. **Ihmaid, S. (2018).** Exploring the Dual Inhibitory Activity of Novel Anthranilic Acid Derivatives towards α-Glucosidase and Glycogen Phosphorylase Antidiabetic Targets: Design, In Vitro Enzyme Assay, and Docking Studies. *Molecules*, *23*(6), 1304. https://doi.org/10.3390/molecules23061304.
8. **Jukič, M., Rožman, K., Sova, M., Barreteau, H., & Gobec, S. (2019).** Anthranilic Acid Inhibitors of Undecaprenyl Pyrophosphate Synthase (UppS), an Essential Enzyme for Bacterial Cell Wall Biosynthesis. *Frontiers in Microbiology*, *9*, 3322. https://doi.org/10.3389/fmicb.2018.03322.
9. **Kwon, I.-S., Kwak, J. H., Pyo, S., Lee, H.-W., Kim, A., & Schmitz, F. J. (2017).** Oscarellin, an Anthranilic Acid Derivative from a Philippine Sponge, *Oscarella stillans* , as an Inhibitor of Inflammatory Cytokines in Macrophages. *Journal of Natural Products*, *80*(1), 149–155. https://doi.org/10.1021/acs.jnatprod.6b00787.
10. **Matsubara, T., Asako, S., Ilies, L., & Nakamura, E. (2014).** Synthesis of Anthranilic Acid Derivatives through Iron-Catalyzed Ortho Amination of Aromatic Carboxamides with *N* -Chloroamines. *Journal of the American Chemical Society*, *136*(2), 646–649. https://doi.org/10.1021/ja412521k.
11. **Mei, X., August, A. T., & Wolf, C. (2006).** Regioselective Copper-Catalyzed Amination of Chlorobenzoic Acids: Synthesis and Solid-State Structures of *N* -Aryl Anthranilic Acid Derivatives. *The Journal of Organic Chemistry*, *71*(1), 142–149. https://doi.org/10.1021/jo0518809.
12. **Merk, D., Lamers, C., Weber, J., Flesch, D., Gabler, M., Proschak, E., & Schubert-Zsilavecz, M. (2015).** Anthranilic acid derivatives as nuclear receptor modulators—Development of novel PPAR selective and dual PPAR/FXR ligands. *Bioorganic & Medicinal Chemistry*, *23*(3), 499–514. https://doi.org/10.1016/j.bmc.2014.12.013.
13. **Nawaz, M., Abbasi, M. W., Tariq, M., Graham, J. P., Al-Hagri, A.-R. S., Elkarim, A. A., Mohamed, M. E., Nissapatorn, V., Taha, M., & Hisaindee, S. (2022).** Synthesis of metal anthranilate complexes: Catalytic and antipathogenic studies. *BMC Chemistry*, *16*(1), 21. https://doi.org/10.1186/s13065-022-00817-x
14. **Oxenkrug, G. (2016).** *Anthranilic Acid: A Potential Biomarker and Treatment Target for Schizophrenia*.
15. **Prasher, P., & Sharma, M. (2021).** Medicinal chemistry of anthranilic acid derivatives: A mini review. *Drug Development Research*, *82*(7), 945–958. https://doi.org/10.1002/ddr.21842
16. **Schörghuber, J., Geist, L., Bisaccia, M., Weber, F., Konrat, R., & Lichtenecker, R. J. (2017).** Anthranilic acid, the new player in the ensemble of aromatic residue labeling precursor compounds. *Journal of Biomolecular NMR*, *69*(1), 13–22. https://doi.org/10.1007/s10858-017-0129-2.
17. **Schrey, H., Müller, F. J., Harz, P., Rupcic, Z., Stadler, M., & Spiteller, P. (2019).** Nematicidal anthranilic acid derivatives from Laccaria species. *Phytochemistry*, *160*, 85–91. https://doi.org/10.1016/j.phytochem.2019.01.008.