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专论与综述

真菌草酸的代谢和作用研究进展

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摘　要：草酸(oxalic acid)是一种重要的生物代谢产物，广泛分布于植物、动物和微生物中，在不同的生命体中发挥重要功能。本文回顾了国内外关于真菌草酸的相关研究进展。许多真菌能够分泌草酸，包括植物病原真菌、食药用真菌及工业真菌等。草酸作为一种简单的二元羧酸，在真菌中主要通过三羧酸循环途径、乙醛酸循环途径和草酰乙酸途径合成。草酸是真菌产生的一种重要的生物因子，能够影响真菌的生长与发育，还能够通过毒素作用、酸化寄主组织环境、参与细胞壁降解和诱导活性氧产生等作用方式，在真菌与寄主植物的互作中发挥作用，也在真菌的生活史和侵染循环中发挥重要的生物学和病理学作用。本文从草酸的理化特性、代谢途径、产草酸的真菌种类、草酸的作用和草酸相关基因功能等方面进行综述，并对未来真菌草酸研究应关注的问题提出了建议。

关键词：真菌；草酸；代谢；致病性；胁迫

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Research progress on metabolism and function of fungal oxalic acid

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Abstract: Oxalic acid, a metabolite with important functions, is ubiquitous in plants, animals, and microorganisms. Many fungi have been reported to be able to secrete oxalic acid, including plant pathogenic fungi, edible and medicinal fungi, and industrial fungi. Oxalic acid as a simple dicarboxylic acid is synthesized in fungi mainly through tricarboxylic acid cycle, glyoxylate cycle, and oxaloacetate pathway. Oxalic acid is an important biological factor produced by fungi, which not only affects the growth and development of fungi but also plays a role in fungus-plant interactions through toxin action, acidification of host plant tissue environment, participation in cell wall degradation, and induction of reactive oxygen species production. Therefore, it is essential in the life cycle and infection cycle of fungi. This paper reviews the properties and metabolism of oxalic acid, the oxalic acid-producing fungal species, the role of oxalic acid and oxalic acid-related genes in these species. Furthermore, we put forward the questions to be solved in the related research, aiming to provide scientific references for the utilization of the fungal resources producing oxalic acid and research ideas for the integrated management of plant fungal diseases.

Keywords: fungi; oxalic acid; metabolism; pathogenicity; stress

草酸(oxalic acid，OA)是一种广泛存在于动物、植物和微生物等生物体内的重要代谢产物[1]。真菌能够合成并分泌草酸以维持生存环境中适宜的 pH 值[2]。草酸在真菌生长发育、环境(生物和非生物因素)胁迫响应等方面发挥重要作用[3-5]。

1 草酸理化特性

草酸又称乙二酸，作为众多有机强酸中一种最简单的二元羧酸，易溶于乙醇，可溶于水，微溶于乙醚，不溶于苯和氯仿等有机溶剂。草酸是无色透明晶体或粉末，通常以二水化合物($H_2C_2O_4·2H_2O$)形态存在于自然界，具有 2 种晶体结构形态(菱形的 α 型和单斜晶形的 β 型)，相对密度约为 1.65，晶体折射率为 1.54[6]。草酸在 190 °C 或遇浓硫酸时分解成二氧化碳(CO_2)、一氧化碳(CO)及水[7]。草酸的酸度比醋酸强约 10 000 倍，具有酸的通性，也是一种强还原剂。草酸还具有毒性和腐蚀性，也是一种强螯合剂，能够与金属离子(如钙离子 Ca^{2+})等螯合形成草酸盐(如草酸钙等)[2]。其中，真菌中草酸通常以草酸盐的形态存在[8]。

2 草酸代谢途径

草酸是生物体内一种重要的代谢产物[1]。植物草酸的合成途径主要包括乙醛酸/乙醇酸途径、抗坏血酸途径和草酰乙酸途径[9-10]。不同于植物，真菌草酸的合成途径主要包括三羧酸循环(tricarboxylic acid cycle，TCA)、乙醛酸循环(glyoxylic acid cycle，GAC)和草酰乙酸途径(图 1)[2,11]，其中草

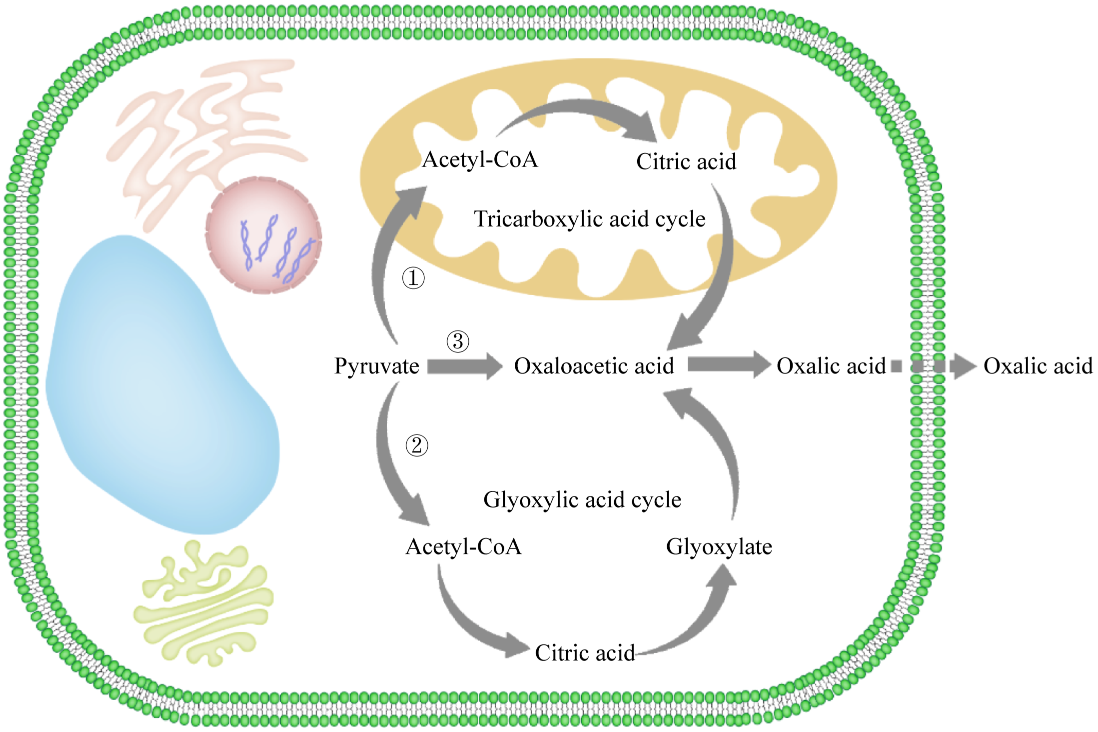

图 1　真菌草酸合成　①：三羧酸循环途径；②：乙醛酸循环途径；③：草酰乙酸途径

Figure 1　Synthesis of oxalic acid in fungi. ①: Tricarboxylic acid cycle pathway; ②: Glyoxylic acid cycle pathway; ③: Oxaloacetic acid pathway.

酰乙酸途径的起源尚未明确[12]。真菌草酸合成的相关研究开展较早，1877 年首次报道在 27 种真菌培养基中检测到草酸[13]。1900 年在酿酒酵母(*Saccharomyces cerevisiae*)的液体培养基中也发现了草酸，随后陆续发现众多真菌能够合成草酸[14]。真菌中影响草酸生物合成的因素主要包括碳源、氮源等营养条件及 pH 值等环境因素[11]。例如，寄生隐丛赤壳(*Cryphonectria parasitica*)在以碳酸钙为碳源的培养基中产生的草酸最多，在 pH 值达到 5.0 及以上时积累大量草酸[15]。同时，草酸的产生也与多种酶有关。例如，核盘菌(*Sclerotinia sclerotiorum*)的草酸合成主要通过草酰乙酸乙酰水解酶(oxaloacetate acetylhydrolase，OAH)催化水解草酰乙酸(oxaloacetic acid)生成草酸[16]。此外，核盘菌的过氧化物酶体系内的肉碱乙酰转移酶(carnitine acetyl transferase，CAT)也参与调控草酸的合成[4]。

草酸的降解主要有氧化和脱羧 2 种途径。其中，氧化途径由草酸氧化酶(oxalate oxidase，OXO)催化，使草酸转化为二氧化碳(CO_2)和过氧化氢(H_2O_2)，主要存在于部分真菌如淡黄褐栓菌(*Trametes ochracea*)和小麦矮腥黑粉菌(*Tilletia contraversa*)中[17]；而脱羧途径主要存在于部分真菌如黑曲霉(*Aspergillus niger*)和绵腐卧孔菌(*Postia placenta*)内，通过草酸脱羧酶(oxalate decarboxylase，ODC)使草酸转化为甲酸(HCOOH)和二氧化碳(CO_2)[18]。例如，在环境 pH 呈酸性条件下，黑曲霉(*A. niger*，pH 1.1)的 ODC 活性被诱导增加，以降低 OA 等无机酸对生长的抑制作用[19]；绵腐卧孔菌(*Postia placenta*)通过 ODC 降

解草酸，调节细胞内和菌丝周围的草酸浓度[11]。另外，真菌草酸降解途径作为靶标已用于真菌病害的防治。通过调控植物的 OXO 和 ODC 表达分解草酸，减弱草酸作用，抵御病原真菌的侵染，提高植物抗性[20-21]。例如，过表达 OXO 基因的转基因番茄对草酸具有较高的耐受性，活性氧的积累能力增强，对灰霉病和菌核病的抗性提高[22]，转基因大豆也具有明显的抗菌核病性状[23-24]。此外，过表达 ODC 基因的转基因番茄和莴苣对核盘菌具有显著的抗性[25-26]。

3 产草酸真菌

文献检索(1877−2021 年)统计结果表明，多种真菌能够产生草酸。产草酸真菌的种类主要属于子囊菌门和担子菌门。其中，植物病原真菌主要包括：引起玉米、高粱、花生、苹果等腐烂病[27]的曲霉属(*Aspergillus*)真菌，导致番茄、瓜类、烟草和豆科等灰霉病[28]的葡萄孢属(*Botrytis*)真菌，造成向日葵、油菜、大豆等油料作物及郁金香等园艺作物菌核病[29]的核盘菌属(*Sclerotinia*)真菌。此外，一些菌根真菌如网褶菌属(*Paxillus*)[30]、部分降解木质素的工业真菌如栓孔菌属(*Trametes*)[11]及少量食用菌如金钱菌属(*Collybia*)[31]也能够产生草酸。详细信息见表 1。

4 真菌草酸的作用

4.1 影响真菌的生长与发育

研究表明，草酸能够影响真菌的生长与发育[62]。例如，核盘菌通过产生草酸以营造适宜菌核发育的酸性环境，实现对不良环境的抗逆性[63-64]。核盘菌菌核渗出液中的草酸可促进真菌分泌细胞壁降解酶的活性以降解寄主植物的细胞壁，并为菌核发育提供营养来源[65]。核盘菌分泌的草酸降低环境 pH 值，进而提高丝裂原活化蛋白激酶(mitogen-activated protein kinase，MAPK)的活性，调控菌核的发育[66]；肉碱乙酰转移酶的缺失引起核盘菌 *Ss-oah1* 基因的表达降低，进而草酸分泌减少，导致菌核发育缺陷、附着胞畸形及侵染垫(infection cushion)功能丧失[4]。通过紫外线诱导或同源重组的方法获得的核盘菌 *oah* 基因突变体菌株，表现为草酸合成及菌核形成能力降低[67-68]。此外，绵腐卧孔菌(*P. placenta*)通过分泌 OXO 降解草酸，以维持营养体菌丝周围的 pH 值，避免草酸浓度过高而抑制菌丝生长[11]。草酸还能够抑制重寄生真菌小盾壳霉(*Coniothyrium minitans*)的菌丝生长和孢子萌发，减弱其对核盘菌的重寄生作用[69]。

4.2 参与病原真菌的致病性及与寄主植物互作

草酸是死体营养型(necrotrophic)植物病原真菌侵染植物的关键因素之一，是一种重要的致病或毒性因子[21,36]。草酸通过毒素作用、酸化寄主植物组织环境、参与细胞壁降解和诱导产生活性氧(reactive oxygen species，ROS)等方式，在真菌与寄主植物的互作中发挥重要作用[2,51]。

(1) 毒素特性

草酸具有毒素作用，诱导寄主植物形成与病原真菌(如核盘菌)侵染相似的症状，在真菌侵染过程中发挥重要作用[36]。例如，核盘菌在侵染初期分泌大量草酸，在寄主组织中不断积累；随着侵染部位草酸浓度的不断升高，在胞间层内直接产生毒素作用，引起寄主细胞坏死[70-71]，影响患病植物逆境响应调控[72]。此外，一些植物，如大麦、玉米、燕麦、大米、黑麦和小麦等具有 OXO 活性，可以将真菌分泌的草酸氧化分解为 H_2O_2，既降低草酸的毒素作用，同时产生的 H_2O_2 也不利于病原真菌的侵入及扩展[73]。

表 1 产生草酸的真菌

Table 1 Fungal species that produce oxalic acid

Taxa	Species	Purpose or influence	References
Ascomycota	*Aspergillus fonsecaeus*	Fermentation	[32]
	Aspergillus niger	Stem rot	[33]
	Aspergillus fumigatus	Aspergillosis	[34]
	Aspergillus terreus	Fermentation	[35]
	Aspergillus aculeatus	Fermentation	[35]
	Beauveria bassiana	Insect control	[36]
	Beauveria caledonica	Insect control	[37]
	Botrytis cinerea	Gray mold	[38]
	Cristulariella pyramidalis	Zonate leaf spot	[39]
	Cytospora chrysosperma	Poplar canker	[40]
	Endothia parasitica	Wilt, chestnut blight	[41]
	Leucostoma cincta (*Valsa mali*)	Apple canker	[42]
	Penicillium bilaii	Phosphorus solubilization	[43]
	Penicillium oxalicum	Phosphorus solubilization	[44]
	Saccharomyces cerevisiae	Fermentation	[14]
	Saccharomyces hansenii	Fermentation	[45]
	Sclerotinia sclerotiorum	Sclerotinia disease	[16]
	Sclerotinia trifoliorum	Clover rot	[46]
	Sclerotium cepivorum	White rot	[47]
	Sclerotium glucanicum	Fermentation	[48]
Basidiomycota	*Abortiporus biennis*	Medicinal fungi	[49]
	Ceriporiopsis subvermispora	White rot	[50]
	Collybia velutipes	Edible mushroom	[31]
	Coriolus hirsutus	Medicinal fungi	[18]
	Dichomitus squalens	Lignin degradation	[11]
	Fomitopsis palustris	Medicinal fungi	[51]
	Fomitopsis pinicola	Medicinal fungi	[52]
	Hebeloma cylindrosporum	Mycorrhizal fungi	[30]
	Heterobasidion parviporum	Root or crown rot	[53]
	Paxillus involutus	Medicinal fungi	[30]
	Phanerochaete sanguinea	Lignin degradation	[11]
	Phanerochaete chrysosporium	Lignin degradation	[54]
	Physisporinus rivulosus	Poisonous mushroom	[55]
	Postia placenta	Root rot	[56]
	Rhizopogon roseolus	Medicinal fungi	[30]
	Rhizoctonia solani	Rice sheath blight	[57]
	Sclerotium rolfsii	Blight	[58]
	Suillus collinitus	Edible mushroom	[30]
	Tilletia contraversa	Dwarf bunt of wheat	[59]
	Tilletia indica	Karnal bunt	[60]
	Trametes ochracea	Lignin degradation	[11]
	Trametes versicolor	Lignin degradation	[11]
	Wolfiporia cocos	Medicinal fungi	[61]

(2) 酸化作用

真菌通过分泌草酸营造有利于侵染的酸性环境[70]。例如，核盘菌在侵染初期分泌草酸，酸化寄主细胞环境，利于病原菌侵染[74-75]。随着寄主植物细胞环境酸度增加，细胞膜的脂质过氧化水平也随之升高，进而改变细胞的通透性，导致细胞丧失水分并引起细胞器结构损伤，加速细胞死亡[16,76]。草酸可调节植物保卫细胞(guard cell)的开放。病原真菌分泌并积累草酸，调控离子(如 K^+)通道，干扰脱落酸(abscisic acid)诱导的气孔关闭，利于病原真菌侵入寄主植物[74]。在病原菌侵染过程中，真菌分泌的草酸诱导寄主植物的 ROS 反应及细胞程序性死亡(programmed cell death，PCD)[21]。此外，草酸与磷酸根离子(PO_4^{3-})存在显著正相关性，菌根真菌(mycorrhiza)分泌的草酸能够增强土壤中磷元素溶解和流动[77]。例如，草酸青霉(*P. oxalicum*)和黑曲霉(*A. niger*)能够通过产生草酸营造酸性环境以提高难溶性磷化合物的溶解[44]。许多菌根真菌通过分泌草酸与铵离子结合形成草酸铵(ammonium oxalate)，实现对重金属离子(如铅、铜和锌离子)的耐受性[8]。另外，菌根真菌分泌的草酸也加速土壤风化，提高伴生植物吸收营养的有效性[2]。例如，真菌草酸通过螯合土壤中的铝和铁影响铝离子和铁离子的运输，促使磷酸盐易被植物根系吸收[78-80]。

(3) 细胞壁降解酶的酶促活性

植物细胞壁具有抵御病原真菌侵染及逆境的作用[81]，而植物病原真菌的侵染和定殖通常与寄主的细胞壁降解相关[58]。植物病原真菌致病过程中产生细胞壁降解酶类(cell wall degrading enzyme，CWDE)如纤维素酶(cellulase)、木质素降解酶(lignin degrading enzyme)、果胶酶(pectinase)和多聚半乳糖醛酸酶(polygalacturonase，PG)等，降解寄主植物角质层和细胞壁，实现侵染与扩展[82]。随着病原菌的侵染及定殖，草酸的积累导致 CWDE 活性增强，进而促进真菌侵入及病害扩展[83]。例如，真菌分泌的 PG 有助于真菌的侵入和定殖，而真菌分泌的草酸能够将寄主组织的 pH 值降至 PG 活性适宜水平[84-85]。典型的死体营养型植物病原真菌(如核盘菌和灰霉菌)通过分泌草酸可将侵染部位细胞环境 pH 值降至 5.0 左右，而这类真菌所产生的 CWDE (如 PG)活性最适 pH 值一般小于 6.0[86]。真菌草酸发挥协同作用，使立枯丝核菌(*R. solani*)和齐整小核菌(*S. rolfsii*)分泌的 PG 更易水解寄主植物果胶层，有助于病原菌的侵入[87]。此外，真菌草酸也通过螯合植物细胞壁的钙离子形成草酸钙晶体，创造有助于真菌侵入寄主细胞角质层的环境，加速患病组织的细胞壁降解，破坏寄主植物细胞壁完整性及免疫反应[2,88]。草酸还能够影响植物产生的抑制真菌 PG 活性的蛋白(如 polygalacturonase-inhibiting protein，PGIP)活性，从而逃避植物防卫反应[89]。

(4) 诱导活性氧产生

植物病原真菌侵染寄主过程中，草酸作用具有两面性[5]。一方面，草酸在侵染过程中诱导寄主植物产生 ROS，促进核盘菌的侵染[66]；另一方面，草酸抑制寄主植物氧暴发反应，改变寄主体内氧化还原水平，解除寄主的防卫反应，诱导寄主 PCD 实现真菌的侵染和扩展[68]。例如，核盘菌分泌的草酸降低患病细胞环境 pH 值或螯合钙离子来抑制寄主的氧暴发反应，或直接抑制氧暴发相关的多酚氧化酶(polyphenol oxidase)、阻断氧化酶激活的识别信号转导，降低寄主的抗性[21,90]。此外，核盘菌侵染过程中，草酸发挥动态调控作用。核盘菌侵染初期，草酸抑制 ROS 产生和胼胝质(callose)沉积等防卫反应；而侵染后期，草酸诱导寄主的 ROS 水平升高，诱发寄主细胞的 PCD 反应，促进腐生性病原菌在寄主

内的进一步扩展[63]。蛋白质组水平分析也表明，草酸通过调控 ROS 与植物激素信号网络，诱导寄主植物产生抗性[72]。因此，低浓度草酸已用于抗灰霉病的番茄品种选育[91]。

5 草酸相关基因功能

植物病原真菌的草酸合成及其他相关调控基因的功能研究逐渐开展，主要影响真菌的草酸代谢、生长和发育和致病性等。其中，真菌草酸合成相关基因研究表明，核盘菌 *Ssoah* 基因突变导致草酸无法产生且菌核形成受阻[68]。近期有研究发现 microRNA-like RNA 通过靶向草酸相关基因(如 *oah*)参与核盘菌草酸合成与调控[92]。灰霉菌 *BcOah* 基因敲除后致病性减弱和毒性降低[28]。金黄壳囊孢菌(*Cytospora chrysosperma*)的 *CcOah* 缺失，导致无法合成草酸、分生孢子数量减少、毒性显著降低[40]。真菌草酸降解相关基因具有重要的作用，例如核盘菌 *Ss-odc2* 基因敲除后草酸和致病性显著降低[93]。此外，一些基因也影响真菌草酸的产生，例如核盘菌 *Ss-Caf1* 和 *SsSOD1* 基因敲除后草酸分泌的能力明显下降，生长发育及致病性等也显著受阻[94-95]。核盘菌黑色素合成途径 *SCD1* 和 *THR1* 基因缺失能够降低草酸的产生，影响菌核发育[96]。黑曲霉 *OAH* 基因敲除后草酸的合成完全被阻断[27]，过表达 *oahA* 基因的黑曲霉的草酸产量约为野生型菌株的 2 倍[33]。详细信息见表 2。

6 展望

真菌分泌的草酸具有多种功能和作用，在真菌的生长发育及侵染寄主植物等方面具有重要意义。本文梳理了真菌草酸的理化特性、代谢途径、产草酸真菌种类、作用影响及相关基因功能等研究进展，总结了草酸在真菌的生长发育和致病机制等方面的重要作用，但关于真菌草酸的系统性研究仍有待加强。未来真菌草酸研究的开展

表 2 草酸的功能与调控

Table 2 Function and regulation of oxalic acid

Taxa	Gene	Function	Method	References
S. sclerotiorum	*Ss-oah1*	Pathogenicity	Knockout	[29]
S. sclerotiorum	–	Pathogenicity	Knockout	[67]
S. sclerotiorum	*sod1*	Pathogenicity	Knockout	[97]
S. sclerotiorum	*Ss-pth2*	Growth, development and pathogenicity	Knockout	[4]
S. sclerotiorum	*Ssoah*	Development, pathogenicity and toxicity	Knockout	[68]
S. sclerotiorum	*pac1*	Pathogenicity and toxicity	Knockout	[75]
S. sclerotiorum	–	Pathogenicity	Knockout	[64]
S. sclerotiorum	*Ss-odc2*	Development and pathogenicity	Knockout	[93]
S. sclerotiorum	*Ss-Caf1*	Growth, development and pathogenicity	T-DNA insertion	[94]
S. sclerotiorum	*SsSOD1*	Development and pathogenicity	Knockout	[95]
S. sclerotiorum	*SCD1*	Development and pathogenicity	Knockout	[96]
S. sclerotiorum	*THR1*	Development and pathogenicity	Knockout	[96]
A. niger	*OAH*	Oxalic acid synthesis	Knockout	[27]
A. niger	*oahA*	Oxalic acid synthesis	Overexpression	[33]
B. cinerea	*BcOah*	Pathogenicity and toxicity	Knockout	[28]
C. chrysosperma	*CcOah*	Development and toxicity	Knockout	[40]

Note: –: No gene.

应关注以下几个方面；(1) 产生草酸的真菌资源调研与利用范围有待拓展，特别是模式真菌及重要植物病原真菌；(2) 真菌草酸的完整合成途径及调控机制仍有待明确，如草酰乙酸途径源于TCA 或 GAC 或两者尚未解析；(3) 草酸对真菌生命活动的作用仍有待系统性开展，包括高通量组学分析发掘大数据信息并构建调控网络或发掘重要因子，采用多种技术(如基因敲除、RNAi 沉默、CRISPR/Cas 等)明确基因功能等；(4) 产生草酸的植物病原真菌引起的作物病害绿色防控方法有限，随着农药过量使用、环境污染及抗药性发生等问题不断出现，加快探索植物病原真菌的致病机理与重要致病因子(如草酸)的生物学功能具有重要意义。

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