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Appendix

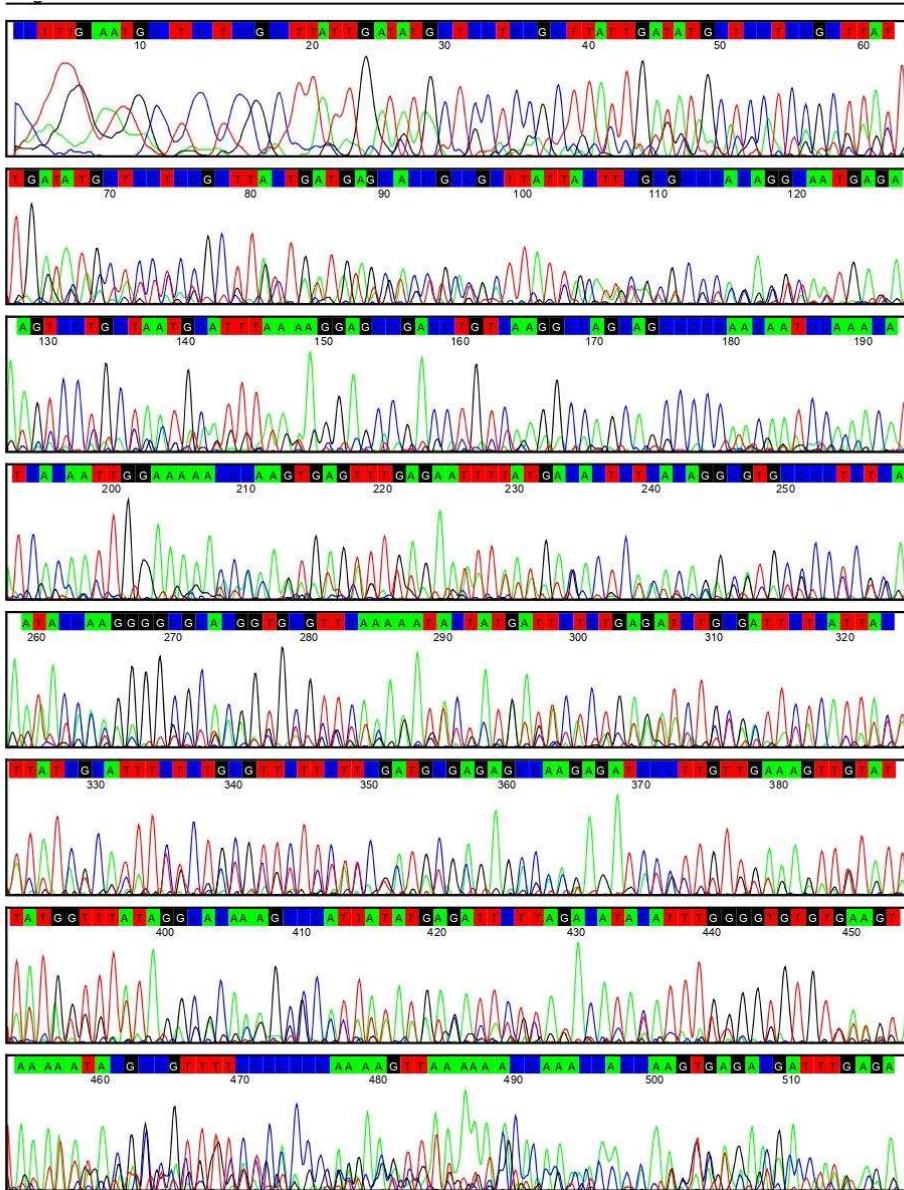


Figure A1. Chromatogram of ITS query sequences of pure culture of *Pleurotus osteratus*.

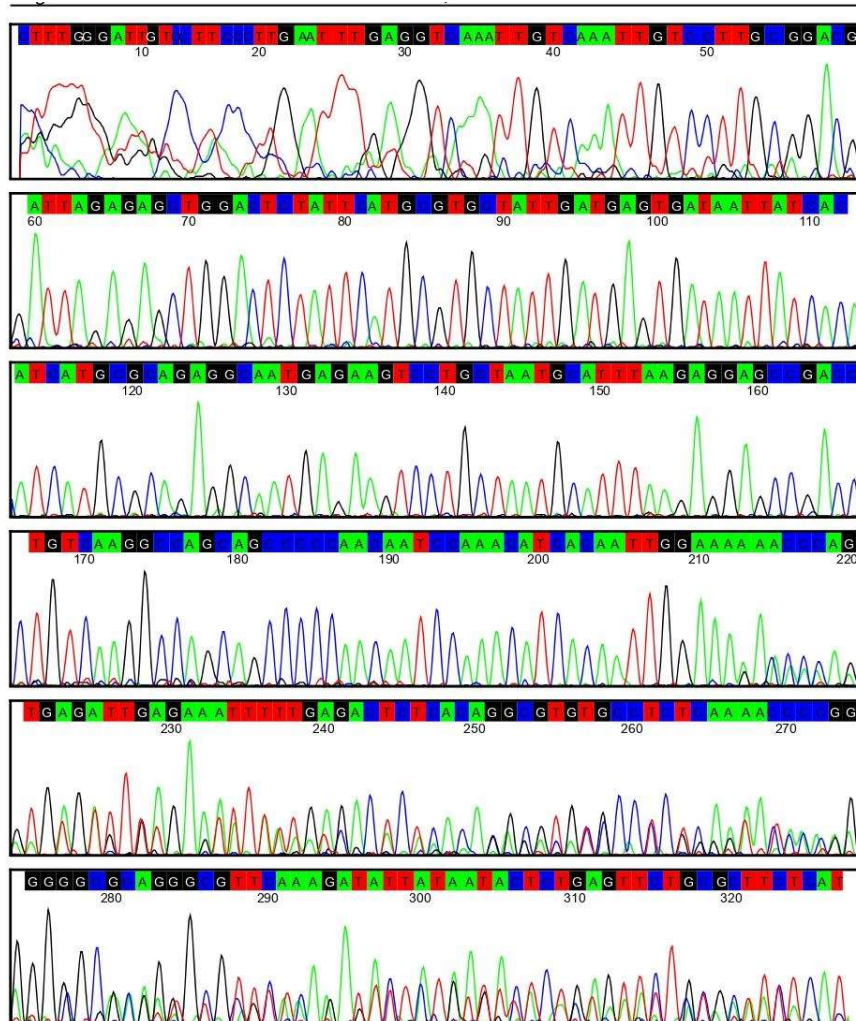


Figure A2. Chromatogram of ITS query sequences of fresh *Pleurotus osteratus* mushroom.

कीटनाशक सूत्रीकरण प्रौद्योगिकी संस्थान
 रसायन एवं पेट्रोसायन विभाग
 रसायन एवं उर्वरक मंत्रालय, भारत सरकार
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TEST REPORT

Report No.: IPFT/ Analytical/21-22/28C

Date: 28/12/2021

Customer details:
 Singh Shreya Hariawadisingh
 c/o Alakh N Sahu
 Associate Professor
 Dept of Pharmaceutical Engg. & Tech.
 IIT (BHU), Varanasi-221005, (India)
 Email: ans@iitbhu.ac.in
 Reference: Your letter dated:- 29/11/2021
 Tel/Mob.: +91-9451137862

Test item/ Sample Details:	
Type of the sample	: R&D Sample
Sample name & ID	: H Sample- Hexane
Batch no.	: NA
Manufactured/ Packed on	: NA
Expiry date	: NA
Date of receipt of sample	: 15.12,2021
Job reference no.	: IPFT/ 28C/21-22
Sampling details	: Sampling was not carried out by IPFT
Condition of samples at receipt	: Good condition
Date of analysis	: 22 Dec-26 Dec 2021

Test Results

Sl No.	Test Parameters	Result	Unit	Test method
1.	Hexane content	BDL	-	GC-MS/MS HS
2.	Volatile Metabolite content	BDL	-	GC-MS/MS HS

BDL: Below Detection Limit (50 µg/kg)

Dr. Subrata Biswas Analyst	Dr. Samsul Alam Technical Manager	Dr. L. K. Thakur Quality Manager

The result listed refers only to the tested sample and application parameters. Endorsement of the product is neither inferred nor implied. Total liability of our institute is limited to the invoice amount only. Pesticide residue test sample will be disposed of after one month and pesticide formulation/ technical samples will be disposed of after one year from the date of issue of test report unless otherwise specified. The report is not to be reproduced wholly or in part and should not be used in an advertising media without our special permission in writing.

Figure A3. GC-HS analysis report on hexane residual content of HFPO1.

कृषि विज्ञान संस्थान

रसायन एवं पेट्रो रसायन विभाग
 रसायन एवं उर्वरक मंत्रालय, भारत सरकार
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Institute of Pesticide Formulation Technology

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 Ministry of Chemicals & Fertilizers, Govt. of India
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TEST REPORT

Report No.: IPFT/ Analytical/21-22/28B

Date: 28/12/2021

Customer details:	
Singh Shreya Hariawadsingh	
c/o Alakh N Sahu	
Associate Professor	
Dept. of Pharmaceutical Engg. & Tech.	
IIT(BHU), Varanasi-221005, (India)	
Email: ansahu.phe@iitbhu.ac.in	Tel/Mob: +91-9451137862
Reference: Your letter dated:- 29/11/2021	

Test item/ Sample Details:	
Type of the sample	: R&D Sample
Sample name & ID	: EA Sample- Ethyl Acetate
Batch no.	: NA
Manufactured/ Packed on	: NA
Expiry date	: NA
Date of receipt of sample	: 15.12.2021
Job reference no.	: IPFT/ 28B/21-22
Sampling details	: Sampling was not carried out by IPFT
Condition of samples at receipt	: Good condition
Date of analysis	: 22 Dec-26 Dec 2021

Test Results				
Sl. No.	Test Parameters	Result	Unit	Test method
1	Ethyl Acetate content	BDL	-	GC-MS/MS HS
2	Volatile Metabolite content	BDL	-	GC-MS/MS HS

BDL: Below Detection Limit (50 µg/kg)

<i>Subrata Biswas</i>	<i>Samsul Alam</i>	<i>L. K. Thakur</i>
Dr. Subrata Biswas	Dr. Samsul Alam	Dr. L. K. Thakur
Analyst	Technical Manager	Quality Manager

The result listed refers only to the tested sample and application parameters. Endorsement of the product is neither inferred nor implied. Total liability of our institute is limited to the invoice amount only. Pesticide residue test sample will be disposed of after one month and pesticide formulation/ technical samples will be disposed of after one year from the date of issue of test report unless otherwise specified. The report is not to be reproduced wholly or in part and should not be used in an advertising media without our special permission in writing.

Figure A4. GC-HS analysis report on hexane residual content of EFPO1.

BANARAS HINDU UNIVERSITY
FACULTY OF MEDICINE
INSTITUTE OF MEDICAL SCIENCES
VARANASI 221 005
(542/GO/ReBi//S/02/CPCSEA dated 26.5.2017)

No. Dean/2021/IAEC/१५५३

Dated: 07.03.2021

Dr. A N Sahu
Associate Professor
Department of Pharmaceutical Engineering & Technology
Indian Institute of Technology
Banaras Hindu University

Dear Sir,

A meeting of the Central Animal Ethical Committee of the University was held on 07.03.2021 at 10.30 AM in the Chamber of the Dean, Faculty of Medicine, IMS for animal ethical clearance of the proposal submitted by the following.

Name of the Student	Singh Shreya H.
Title	Evaluation of LD50, Acute toxicity & Anti-cancer activity of Pleurotus osteratus fractionate
No. of Animals Approved	Swiss Mice- 90
Suggestion	The CPCSEA Guidelines should be followed strictly while handling the animals
Remarks	The Study is approved by the Central Animal Ethical Committee of the University

This is for your information and necessary action at your end.

Yours sincerely,



(B K DAS)
DEAN
&
CHAIRMAN

CENTRAL ANIMAL ETHICAL COMMITTEE OF THE UNIVERSITY

Figure A5. Institutional Animal Ethics Committee Approval.

AOT425statpgm (Version: 1.0) Test Results and Recommendations
Acute Oral Toxicity (OECD Test Guideline 425) Statistical Program

Date/Time: 15 February 2021, 10:58:24
Data file name: HEXANE FRACTION.dat
Last modified: 15-02-2021 10:57:17

Test/Substance: Enter test description.
Test type: Main Test
Limit dose (mg/kg): 2000
Assumed LD50 (mg/kg): Default
Assumed sigma (mg/kg): 0.5

Recommended dose progression: 2000, 550, 175, 55, 17.5, 5.5, 1.75

DATA:

Test Seq.	Animal ID	Dose (mg/kg)	Short-term Result	Long-term Result
1	H-1	175	0	0
2	H-2	550	X	X
3	H-3	2000	X	X
4	H-4	550	X	X
5	H-5	175	0	0
6	H-6	550	X	X
7	H-7	175	0	0
8	H-8	550	X	X
9	H-9	175	0	0

(X = Died, 0 = Survived)

Dose Recommendation: The main test is complete.

WARNING:

Please review the data for accuracy.
A death should be followed by a lower dose and a survival by a higher dose.
The doses are not completely consistent with the recommended doses.

Stopping criteria met: 5 reversals in 6 tests.

SUMMARY OF LONG-TERM RESULTS:

Dose	0	X	Total
175	4	0	4
550	0	4	4
2000	0	1	1
All Doses	4	5	9

Statistical Estimate based on long term outcomes:

Estimated LD50 = 301 (Based on an assumed sigma of 0.5).
Approximate 95% confidence interval is 175 to 550.

Figure A6. Acute oral toxicity (OECD 425) based estimated LD₅₀ of HFPO1.

Test/Substance: Enter test description.

Test type: Main Test

Limit dose (mg/kg): 2000

Assumed LD50 (mg/kg): Default

Assumed sigma (mg/kg): 0.5

Recommended dose progression: 2000, 550, 175, 55, 17.5, 5.5, 1.75

DATA:

Test Seq.	Animal ID	Dose (mg/kg)	Short-term Result	Long-term Result
1	1	175	O	O
2	2	550	O	O
3	3	2000	X	X
4	4	550	O	X
5	5	2000	X	X
6	6	550	O	X
7	7	2000	X	X

(X = Died, O = Survived)

Dose Recommendation: The main test is complete.

Stopping criteria met: 5 reversals in 6 tests.

SUMMARY OF LONG-TERM RESULTS:

Dose	O	X	Total
175	1	0	1
550	1	2	3
2000	0	3	3
All Doses	2	5	7

Statistical Estimate based on long term outcomes:

Estimated LD50 = 550 (The one dose with partial response).
95% PL Confidence interval is 3.325 to 1020.

Figure A7. Acute oral toxicity (OECD 425) based estimated LD₅₀ of EFPO1.

Publication

Research paper

- **Shreya Singh**, Dulla Naveen Kumar, Debadatta Mohapatra, Shivani Jaiswal, Gaurav Gopal Naik, Santosh Kumar Guru, Ashish Kumar Agarwal, Senthil Raja Ayyannan, and Alakh N. Sahu. (2022). Tracing the Anti-Cancer Mechanism of *Pleurotus osteratus* by the Integrative Approach of Network Pharmacology and Experimental Studies. *Applied Biochemistry and Biotechnology*, 195(1), pp.152-171. <https://doi.org/10.1007/s12010-022-04111-3> **(Published)**
- **Shreya Singh**, Debadatta Mohapatra, Gaurav Gopal Naik, Yamini Bobde, Balaram Ghosh, and Alakh N Sahu. (2023). In-Vitro Antioxidant and Cytotoxic Potential of *Pleurotus* Mushroom and Activity-based Correlation: A Comparative Study. 78(4), 456-463. <https://doi.org/10.1134/S1061934823040135> **(Published)**
- **Shreya Singh**, Deepak Kasote, Debadatta Mohapatra, Gaurav Gopal Naik, Santosh Kumar Guru, Nese Sreenivasulu, Yashpal Sharma, and Alakh N. Sahu. (2023). Chemometric-based analysis of metabolomics of bioactive enriched fractions of *Pleurotus osteratus* and their correlation with in-vitro anti-cancer activity. *Applied Biochemistry and Biotechnology*, 1-15. <https://doi.org/10.1007/s12010-023-04325-z> **(Published)**
- **Shreya Singh**, Dulla Naveen Kumar, Debadatta Mohapatra, Gaurav Gopal Naik, Santosh Kumar Guru, Ashish Kumar Agarwal, and Alakh N. Sahu. Tracing the Anti-Cancer Mechanism of *Pleurotus osteratus* fractionate by the Integrative Approach of Network Pharmacology and Experimental Studies. **(Under communication)**

Review paper

- **Shreya Singh**, Shreyans Kumar Jain, Santosh Kumar Guru, and Alakh N. Sahu. (2022). Anti-cancer potential of *Pleurotus* mushroom: Detailed insight on the potential bioactive molecules, In-vitro – In-vivo studies, and formulation. *Letter in Drug Design & Discovery*, 20(4), 439-456. <https://dx.doi.org/10.2174/1570180819666220518100010> **(Published)**