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Abbreviations

Sl. No.	Abbreviations Used	Full Form
1	GABA	Gamma-Aminobutyric Acid
2	TCM	Traditional Chinese Medicine
3	SARS	Serious Acute Respiratory Syndrome
4	ITS	Internal Transcribed Spacer
5	CA	Cordycepic Acid
6	NMR	Nuclear Magnetic Resonance
7	IR	Infrared Spectroscopy
8	PLE	Pressurized Fluid Extraction
9	TMS	Trimethyl Silyl
10	VRE	Vancomycin-Resistant Enterococcus
11	EPSF	Exopolysaccharide
12	PS	Polysaccharide
13	PSF	Polysaccharide Fraction
14	CLSs	C-Type Lectin Receptors
15	TLRs	Toll-Like Receptors
16	APCs	Antigen-Presenting Cells
17	TLR4	Toll-Like Receptor 4
18	DC-SIGN	Dendritic Cell-Specific Intercellular Adhesion Molecule-3-Grabbing Non-Integrin
19	SOCS	Suppressor Of Cytokine Signaling
20	PI3K	Phosphatidylinositol-3-Kinase
21	RAF	Rapidly Accelerated Fibrosarcoma
22	MR	Mannose Receptor
23	MGL	Macrophage Galactose-Type C-Type Lectin
24	PBMCs	Peripheral Blood Mononuclear Cells
25	NK	Natural Killer
26	GM-CSF	Granulocyte-Macrophage Colony-Stimulating Factor
27	CMP	C. Militaris Polysaccharides
28	LPS	Lipopolysaccharide
29	NO	Nitric Oxide
30	IgG	Immunoglobulin G
31	JNK	C-Jun N-Terminal Kinase
32	iNOS	Inducible Nitric Oxide Synthase
33	APS	Acidic Polysaccharide
34	MDA	Malondialdehyde
35	mTOR	Mammalian Target Of Rapamycin
36	MMP	Matrix Metallopeptidase
37	XIAP	X-Linked Inhibitor Of Apoptosis Protein

Publications

1. **Biswa, V.,** Ali, R., Pradhan, D. K., Boro, N., Baro, T., Das, D., ... & Das, S. (2021). Molecular characterization, microscopic characteristics, and phylogenetic analysis of *Ophiocordyceps sinensis* from Sikkim, India. *Indian Journal of Hill Farming*, *34*, 268-275.

2. **Biswa, V.,** Ali, R., Boro, N., Namsa, N D., Das, P., ... & Das, S. (2023). First report of *Ophiocordyceps liangshanensis* from Arunachal Pradesh India- Its molecular characterization, phylogenetic studies, nutritional and metabolomic analysis. *Indian Journal of Hill Farming, 36,* 30-36.

3. C., Ayyanar, M., Amalraj, S., Khanal, P., Subramaniyan, **Biswa,V.,** Das, S., ... & Gurav, S. Dias, (2022). Biogenic synthesis of zinc oxide nanoparticles using mushroom fungus *Cordyceps militaris*: Characterization and mechanistic insights of therapeutic investigation. *Journal of Drug Delivery Science and Technology*, 103444.

4. Gandhale, P., Chikhale, R., Khanal, P., **Biswa, V.,** Ali, R., Khan, M. S., ... & Gurav, S. (2024). Quest for Anti-SARS-CoV-2 antiviral therapeutics: in-silico and in-vitro analysis of edible mushroom-*Cordyceps militaris*. *Journal of Ayurveda and Integrative Medicine*, 100979.

5. **Biswa, V.,** Boro, N., Ali, R., & Das, S. · Characterization of two medicinal entomopathogenic fungi from India's Eastern Himalayan belt: *Ophiocordyceps sinensis* and *Ophiocordyceps liangshanensis* for its antioxidant, antimicrobial and anticancer efficacy *(Under Communication)*

Book Chapter

1. **Biswa, V,** Ali, R., & Das, S. Medical values of mushrooms with special reference to entomoparasitic fungi-cordyceps spp. *Life sciences: trends and technology*, 9.

Conference

1. **Biswa, V.**, Ali, R., and Das, S. (2021) "Antioxidant and Metabolomics Study of *Ophiocordyceps sinensis* found in Sikkim, India" at the National Seminar on Ethnobotany and Resource Management of the Bodos, Centre for Bodo Studies, Bodoland University, Kokrajhar, Assam, 10th December, 2021.

2. **Biswa, V.**, Ali, R., and Das, S. (2021) "Molecular Taxonomy of Ethnomopathogenic Fungi *Cordyceps* spp. Found in Eastern Himalayan Region" at the International Conference on Emerging Technologies in Food Processing-III (ETFP-2023), Department of Food Processing Technology, Ghani Khan Choudhury Institute of Engineering and Technology, Narayanpur, Malda, West Bengal, 26th- 27th September, 2023

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Indian Journal of Hill Farming

Special Issue 2021, Volume-34, Page 268-275

Molecular characterization, microscopic characteristics, and phylogenetic analysis of *Ophiocordyceps sinensis* from Sikkim, India

Vashkar Biswa[1] • Raju Ali[1] • Durga Kr. Pradhan[2] • Nitisha Boro[3] • Tikendrajit Baro[1] • Debajani Das[1] • Robin Subba[4] • Puja Das[4] • Sandeep Das[1]

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Key words: *Medicinal Mushroom, Fungi, Taxonomy, Phylogeny, Ophiocordyceps sinensis.*

ABSTRACT

The zombie fungi are a group of entomo-parasitic fungi comprising of 400 diverse species having tremendous pharmaceutical virtues. They have their use in traditional practice among Himalayan highlanders and inhabitants across the globe living in high altitude areas. *Ophiocordyceps sinensis* is one such representative of the entomo-parasitic group. The current study aimed to identify *Ophiocordyceps sinensis* from Sikkim, India, following classical, molecular taxonomic approaches, and culture. The classical approach involved a microscopic study of asci, stroma, and mycelia and the macroscopic characters of the stroma and larva. The molecular approach involved the amplification of internal transcribed spacer (*ITS*) region from the stroma, cytochrome oxidase subunit-I (*COI*), and cytochrome *b* (*Cytb*) from host larva for phylogenetic studies. The pure culture was established on potato dextrose agar (PDA). The sequences were edited with Bioedit version 7.2.5 and subjected to multiple alignments using fast fourier transform (MAFFT) database. Model testing was performed using MegaX version 10.2.5, and the best model was utilized to construct the maximum likelihood tree. To confirm the results of the maximum likelihood tree, a Bayesian tree was also constructed using MrBayes 3.2.7. Subsequently, the study confirmed that the collected specimen is *O. sinensis*. The main bioactive compounds of *O. sinensis* are cordycepin and adenosine which has been explored for different therapeutic applications including treatment of cancer, diabetes, anemia, inflammation etc. Thus, such study provides the platform for their exploration for extensive pharmaceutical and nutraceutical future studies.

1. Introduction

Ophiordyceps sinensis (Berk.) is an entomo-pathogenic fungus belonging to the genus *Ascomycota* [Zhou et al. (2014)]. It consists of >400 different species worldwide, which are parasitic, mainly on insects and larvae. Typically, it exists in two stages: an asexual stage (mitosporic fungi) and a sexual stage. The mitosporic fungi are parasitic on dead caterpillars of the moth *Hepialus* spp. The spores of *O. sinensis* germinate inside the caterpillars, colonizing with hyphae and producing a stalked ascomata (sexual stage) [Zeng, W., Yi, D.H. and Huang, T.F. (1998), Pu, Z.L. and Li, Z.Z. (1996)]. *Cordyceps* are mainly found in China, Nepal, and India at 3500 m above sea level. The fungus is a coveted medicinal utility in traditional Tibetan and Chinese medicine, which is commonly known in the West as "Himalayan Viagra." In India, the collection and trade of *Cordyceps* by the Bhotiya community have been reported from Garhwal, Uttarakhand [Caplins, L. B. (2016)]. It has also been reported

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ABSTRACT

The zombie fungi are a group of entomo-parasitic fungi comprising of 400 diverse species having tremendous pharmaceutical virtues. They have their use in traditional practice among Himalayan highlanders and inhabitants across the globe living in high altitude areas. *Ophiocordyceps sinensis* is one such representative of the entomo-parasitic group. The current study aimed to identify *Ophiocordyceps sinensis* from Sikkim, India, following classical, molecular taxonomic approaches, and culture. The classical approach involved a microscopic study of asci, stroma, and mycelia and the macroscopic characters of the stroma and larva. The molecular approach involved the amplification of internal transcribed spacer (*ITS*) region from the stroma, cytochrome oxidase subunit-I (*COI*), and cytochrome *b* (*Cytb*) from host larva for phylogenetic studies. The pure culture was established on potato dextrose agar (PDA). The sequences were edited with Bioedit version 7.2.5 and subjected to multiple alignments using fast fourier transform (MAFFT) database. Model testing was performed using MegaX version 10.2.5, and the best model was utilized to construct the maximum likelihood tree. To confirm the results of the maximum likelihood tree, a Bayesian tree was also constructed using MrBayes 3.2.7. Subsequently, the study confirmed that the collected specimen is *O. sinensis.* The main bioactive compounds of *O. sinensis* are cordycepin and adenosine which has been explored for different therapeutic applications including treatment of cancer, diabetes, anemia, inflammation etc. Thus, such study provides the platform for their exploration for extensive pharmaceutical and nutraceutical future studies.

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Biogenic synthesis of zinc oxide nanoparticles using mushroom fungus *Cordyceps militaris*: Characterization and mechanistic insights of therapeutic investigation

Charmaine Dias [a,1], Muniappan Ayyanar [b,1], Singamoorthy Amalraj [b], Pukar Khanal [c], Vijayakumar Subramaniyan [b], Sandeep Das [d], Pradeep Gandhale [e], Vashkar Biswa [d], Raju Ali [d], Nilambari Gurav [f], Sameer Nadaf [g], Nilesh Rarokar [h], Shailendra Gurav [a,*]

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ARTICLE INFO

Keywords:
Antibacterial
Antidiabetic
Cordyceps militaris
Nanoparticles
Zinc oxide

ABSTRACT

The present research demonstrates the *Cordyceps militaris* (a medicinal mushroom) mediated fabrication of zinc oxide nanoparticles (*Cor*-ZnONPs) and its therapeutic investigation. The biosynthesized *Cor*-ZnONPs were characterized by UV–Visible spectroscopy, FT-IR, XRD, SEM with EDX, HRTEM, particle size, and zeta potential analysis and evaluated for their antidiabetic, antioxidant, and antibacterial potential by *in-vitro* methods. The nanoparticles showed SPR peak at 354 nm. FT-IR analysis exhibited a sharp peak at 432.05 cm^{-1}, demonstrating the distinctive Zn–O bond. *Cor*-ZnONPs had an average particle size of 1.83 nm with a polydispersity index of 0.29 and were crystalline as obtained from XRD analysis. Zeta potential of −6.42 mV indicates the moderate stability of nanoparticles. EDX analysis confirmed the presence of Zinc and Oxygen. *Cor*-ZnONPs expressed a 70–90% survival rate in brine shrimp lethality assay with 10–100 ppm concentrations and exhibited potent α-amylase and α-glucosidase inhibitory effect with an IC_{50} of 46.29 ± 0.49 and 47.21 ± 0.19 μg/mL, respectively. *Cor*-ZnONPs showed moderate radical potency with DPPH, ABTS, hydroxyl radical, nitric oxide, and superoxide radical scavenging assays. *Cor*-ZnONPs revealed the highest antibacterial activity against *Pseudomonas aeruginosa*, followed by *Shigella flexneri*, *Proteus vulgaris*, and *Rhodococcus equi*. Moreover, a very low concentration of *Cor*-ZnONPs was required to inhibit the growth of studied bacterial strains. This study provides an informational insight into the *Cordyceps militaris* mediated synthesis of ZnONPs, and their antidiabetic, antioxidant, and antibacterial potential. Biosynthesized *Cor*-ZnONPs indicate a new application of nanoparticles in the development of therapeutic drugs.

Abbreviations: ZnONPs, Zinc Oxide Nanoparticles; *Cor*-ZnONPs, *Cordyceps militaris* ZnO Nanoparticles; XRD, X-ray Diffraction Study; SEM, Scanning Electron Microscopy; HRTEM, High-Resolution Transmission Electron Microscopy; SAED, Selected Area Electron Diffraction; PSA, Particle size analysis; EDX, Energy dispersive X-ray analysis; PDA, Potato Dextrose Agar; SPR, Surface Plasmon Resonance; ITS, Internal Transcribed Spacer; FT-IR, Fourier Transform Infrared Spectrophotometer; PDI, Polydispersity index; PNPG, p-nitrophenyl-α-D-glucopyranoside; DPPH, 2, 2-diphenyl-1-picrylhydrazyl; ABTS, 2, 2′-azino-bis-(3-ethylbenzothiozoline-6-sulfonic acid) diammonium salt; BHT, Butylated Hydroxy Toluene; ROS, Reactive Oxygen Species.

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Original Research Article (Experimental)

Quest for Anti-SARS-CoV-2 antiviral therapeutics: *in-silico* and *in-vitro* analysis of edible mushroom- *Cordyceps militaris*

Pradeep Gandhale [a,1], Rupesh Chikhale [b,1], Pukar Khanal [c], Vashkar Biswa [d], Raju Ali [d], Mohd Shahnawaz Khan [e], Nilambari Gurav [f], Muniappan Ayyanar [g], Sandeep Das [d], Shailendra Gurav [h,*]

[a] ICAR-National Institute of High-Security Animal Diseases, Bhopal, Madhya Pradesh- 462 021, India
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Covid-19
Molecular docking
Molecular dynamics
Network pharmacology
Edible mushroom

ABSTRACT

Background: The emergence and evolution of SARS-CoV-2 resulted a severe threat to public health globally. Due to the lack of an effective vaccine with durable immunity, the disease transited into the endemic phase, necessitating potent antiviral therapy including a scientific basis for current traditional herbal medicine.
Objective: This study aimed to conduct a pharmacoinformatic analysis of selected chemical ingredients and *in-vitro* evaluation of *Cordyceps militaris* extract against SARS-CoV-2.
Materials and methods: *C. militaris*, the widely used fungus in conventional herbal medicine, was subjected to computational investigation using molecular docking, molecular dynamic simulation and network pharmacology analysis followed by the *in-vitro* assay for evaluating its anti-SARS-CoV-2 potential.
Results: The molecular docking analysis of *C. militaris* revealed the Cordycepin's highest affinity (−9.71 kcal/mol) than other molecules, i.e., Cicadapeptin-I, Cicadapeptin-II, Cordycerebroside-B, and N-Acetyl galactosamine to the receptor binding domain of the SARS-CoV-2 spike protein. *C. militaris* aqueous extract could reduce the SARS-CoV-2 viral copy numbers by 50.24% using crude extract at 100 μg/mL concentration.
Conclusion: These findings suggest that *C. militaris* has promising anti-SARS-CoV-2 activity and may be explored as traditional medicine for managing the COVID-19 surge in the endemic phase.

1. Introduction

Four years after its emergence as multiple severe pneumonia cases in Wuhan, China, in 2019, the severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) still represents a significant global public health threat. Owing to its continuous evolution and rapid spread, till April 30, 2024, there were 7,75,335,916 confirmed cases of COVID-19, with 7,045,569 deaths across the continents (www.covid19.who.int). Even though, as of April 30, 2024, a total of 13.59 billion vaccine doses have been administered worldwide, it still poses a significant challenge to the healthcare system, as evidenced by the recent surge of COVID-19 cases globally [1]. Although COVID-19 is still a pandemic, it may eventually turn endemic. The observed evolution and resurgence of SARS-CoV-2 indicates that the virus is unlikely to go extinct anytime soon in the absence of a vaccine that can provide durable immunity. Therefore, it is likely that the virus will eventually move to an endemic phase, at which point new cases of the infection will arise [2]. Furthermore, the endemicity could result in a new pandemic of long

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[1] Equal contribution.

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(A Centrally Funded Technical Institute, Ministry of Education, Government of India)

Narayanpur, Malda, West Bengal: 732141

Certificate No: ***GKCIET/FPT/ETFP-III/109***

Certificate for Presentation

This is to certify that ***Vashkar Biswa*** *of* ***Bodoland University*** *has given a* ***Oral presentation*** *in the International Conference on* ***"Emerging Technologies in Food Processing-III (ETFP-2023)"*** *organized by the* ***Department of Food Processing Technology****, Ghani Khan Choudhury Institute of Engineering and Technology, Malda, West Bengal during 26th -27th Sept, 2023.*

Title: Molecular taxonomy of entomopathogenic fungi cordyceps spp. Found in eastern himalayan region

Authors: Vashkar Biswa, Raju Ali And Sandeep Das*

Dr Mudasir Ahmad Malik
Organizing Secretary
ETFP-2023

Dr Kshirod Kumar Dash
Organizing Secretary
ETFP-2023

Prof. P R Alapati
Director
GKCIET Malda

Centre for Bodo Studies, Bodoland University

National Seminar on
'Ethnobotany and Resource Management of the Bodos'
(December 10, 2021)

CERTIFICATE

As Paper Presenter

This is to certify that Vashkar Biswa of Bodoland University, Assam, has presented a paper entitled Antioxidant and metabolomics study of Ophiocordyceps sinensis found in Sikkim, India (Author(s): Vashkar Biswa, Raju Ali, Sandeep Das) in the National Seminar organized by the Centre for Bodo Studies, Bodoland University held on 10th December, 2021.

Dr. Prahlad Basumatary
Director
Centre for Bodo Studies
Bodoland University

Prof. Laishram Ladusingh
Vice Chancellor
Bodoland University

CENTRE FOR BODO STUDIES CBS/BU/ERMB2021/1018

CENTRE FOR BODO STUDIES, BODOLAND UNIVERSITY * ETHNOBOTANY AND RESOURCE MANAGEMENT OF BODOS * HELD ON 10TH DECEMBER, 2021 * NATIONAL SEMINAR 2021

BODOLAND UNIVERSITY BOTANICAL HERBARIUM (BUBH)
DEPARTMENT OF BOTANY
BODOLAND UNIVERSITY, KOKRAJHAR
ASSAM-783370

Date: 25.04.2024

To,
Vashkar Biswa
Ph.D Research Scholar
Department of Biotechnology
Bodoland University

Subject: Incorporation of Herbarium specimen at BUBH.

Dear Vashkar,

With reference to your application, dated: 22.04.2024 and the above cited subject the fungal specimens have been incorporated in BUBH with accession numbers as follows.

Sl. No.	Name of the species	Assigned Abbreviation	Accession number
1	*Ophiocordyceps sinensis*	CBUB1	BUBH0000876
2	*Ophiocordyceps sinensis*	CBUB2	BUBH0000877
3	*Ophiocordyceps sinensis*	CBUB3	BUBH0000878
4	*Ophiocordyceps sinensis*	CBUB4	BUBH0000879
5	*Ophiocordyceps liangshanensis*	CBUAP1	BUBH0000880
6	*Ophiocordyceps sinensis*	CBUS1	BUBH0000881
7	*Ophiocordyceps sinensis*	CBUS2	BUBH0000882
8	*Ophiocordyceps sinensis*	CBUS4	BUBH0000883

This is for your kind information

Thanking You

Dr. Sanjib Baruah
Asstt. Prof. Dept of Botany
Bodoland University,
Kokrajhar

Dr. Sanjib Baruah
Assistant Professor
Dept. of Botany
Bodoland University
Kokrajhar-783370

GOVERNMENT OF ARUNACHAL PRADESH

GOVERNMENT OF SIKKIM
DEPARTMENT OF FOREST, ENVIRONMENT & WILDLIFE MANAGEMENT
OFFICE OF THE SECRETARY CUM CHIEF WILDLIFE WARDEN
DEORALI, GANGTOK 737 102
Ph.: (03592) 281261, /Fax: 03592-281778

F. No: 78/GOS/FEWMD/BD-R-2015/ 124 Date: 16 / 02 /2021

RESEARCH PERMIT

With the approval of competent authority and under the provision of the Wild Life (Protection) Act, 1972; Forest (Conservation) Act 1980, Biological Diversity Act, 2002; the rules and regulations framed there under, permission is hereby granted

1. **TO:** Mr. Vashkar Biswa, PHD Scholar, Depart of Biotechnology, Bodoland University.
2. **FROM:** Phd Scholar,Department of Biotechnology,Mushroom Spawn Unit) Bodoland University, Kikrajhar, Assam
3. **FOR PROJECT:** To conduct survey of documentation of wild edible mushrooms found in North Sikkim
4. **PERIOD:** One years

Research Permit holder shall pay separate Entry fees and other charges (if any) to the respective sectors / RFs / WLPAs including National Park / Biosphere Reserve / Zoological Park.

Area where the license / permit is applicable	Details of Project / Research (kind of study) whether collection is required, etc.
Potential area of North Sikkim.	1. Survey and documentation of wild mushrooms collection in the district of North Sikkim

The permit is not transferable.

Sd/-
(Y.P. Gurung,)
Secretary cum Chief Wildlife Warden

Vashkar Biswa
Specimen signature of the permit holder

Copy to:

1. Mr. Vashkar Biswa, PHD Scholar, Depart of Biotechnology, Bodoland University.
2. Secretary-Cum- Chief Wildlife Warden
3. CF(WL),CF(T), CF(W/P), CF(FCA),
4. Member Secretary (SBB)
5. Divisional Forest Officer(T, WL, KNP/KBR) North
6. Assistant Conservator of Forest (T.WL, KNP/KBR) North
7. Office/file Copy

Note: See terms and conditions overleaf

Assistant Conservator of Forest
(Research and Extension)

Assistant Conservator of Forest
Research & Extension
Forest & Environment Deptt.

GOVERTMENT OF ARUNACHAL PRADESH
OFFICE OF THE PRINCIPAL CHIEF CONSERVATOR
OF FORESTS (WL & BD), ITANAGAR.
****

No. CWL/Gen/173/2018-19/Pt.IX/NG 1802-05 Dated.....25th.....May, 2021

To,

Prof. SandeepDas
Technology Incubation Center
Bodolang University
PO & PS- Kokrajar
Assam, 783370

Email: sandeep_dna2003&yahoo.co.in
(M): 8638779415

Sub: Research Permission
Ref: Your Application No.NG/24 dated 20/04/2021

Sir,

With reference to your application no. mentioned above, I am directed to convey the approval of the CWLW for the research project under section 28 (1) (a),(b), (c) of the Wildlife (Protection) Act, 1972 (Amended upto 2006).

Further, it is to mention that under no circumstances shall collection of species listed under Schedule 1 and Schedule VI of the Wildlife (protection), Act 1972 be made without permission of the central Government. The research activities are strictly governed by guidelines issued by the Department of Environment & Forests, Govt. of Arunachal Pradesh for scientific research in Protected Areas (PAs) and other forest areas of Arunachal Pradesh vide notification No.CWL/GEN/190/2019/Pt/3204-47 dated 1st March 2021. This permission is valid for a period of one year from the date of issue of this letter. Subsequent extension of the permit will be made on submission of the interim report and payment of the annual research fees.

Yours faithfully

DCF (BR & ET)
O/o the PCCF (WL & BD)
Itanagar.

Copy to: The DFOs Tawang, Bomdila, Allo for information and necessary action.

DCF (BR & ET)
O/o the PCCF (WL & BD)
Itanagar.