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Research Article

Agaricus Bisporus Show Effect on Anti-Depressant

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ABSTRACT

Many important nutrients and medicinal bioactive chemicals are thought to be possible to be found in mushrooms. Agaricus bisporus is the most significant commercially grown mushroom worldwide and a member of the Basidiomycetes family. Rich in minerals, vitamins, lipids, fiber, proteins, and carbohydrates, this mushroom is a well-known nutritious food. Mirtazapine is a commonly prescribed antidepressant medication that is a member of the BCS Class II drug class and has high permeability and low solubility. Goal: The formulation of the gastroprotective floating tablets of mirtazapine was statistically optimized using the Box Behnken design. Materials and Procedures: Using design expert software, a polynomial model was created after the responses were examined using the three components of the three design levels. A comparison was made between three distinct independent components. Reviewing contemporary research on the nutritional and therapeutic qualities of Agaricus bisporus is the primary aim of this research. Only findings released after 2006 have been taken into consideration due to the acceleration of mushroom research during the past 10 years. The maintenance of human health has relied heavily on the use of therapeutic substances derived from plants and fungi from ancient times. Natural products are the source of more than half of all contemporary clinical medications and are crucial to pharmaceutical industry drug research initiatives. A significant natural food and medicinal source is mushrooms. The significance of edible and wild mushrooms was recognized by traditional Aboriginal people, and these are currently being examined for their bioactivity in treating a range of illnesses. This review's objective is to provide a concise scientific explanation of the pharmacognosy, chemistry, and pharmacology of button mushrooms.

INTRODUCTION

Globally, mushrooms are already a significant component of human diets as non-animal sources

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of protein, but less is known about their environmental impact and value chain. A controlled drug delivery system is utilized to improve a medicine's therapeutic efficacy and get around some issues with traditional therapy(1). A member of the kingdom's Agaricaceae family, division Basidiomycota of fungi, Agaricus bisporus Imbach is one of the most widely grown mushrooms around the world. Champignon, button, and white mushrooms are some of the common names for this species. In this essay, the word "mushroom" will be used instead. Apart from its medicinal and cosmetic uses, this fungus is primarily consumed by humans. It is extremely nutritious because it is a source of (2). The agent must be delivered to the target tissue in the ideal quantity at the ideal timing in order to achieve optimum therapeutic efficacy, resulting in low toxicity and few adverse effects. Delivering a medicinal ingredient to the target site in a prolonged controlled release form can be accomplished in a number of ways.Microspheres are tiny spherical particles that usually have dimensions between 1 μm and 1000 μm, which is in the micrometer range. Microspheres can also be called microparticles. A variety of synthetic and natural materials are used to make it. Commercially available microspheres come in three varieties: glass, polymer, and ceramic(3). in order to create microspheres using a variety of natural and artificial materials. Commercially available Since ancient times, mushrooms have been valued as a food item due to their nutritional content and medicinal qualities. The mushroom was used as food and medicine in ancient China, where people thought it established human body and health and preserved youth for as long as possible (Safwat and Al Kholi, 2006)(4). The Egyptians thought that mushrooms were a gift from the god Osiris, while the Greeks thought that they gave warriors vigor during combat (Daba et al., 2008). (Maihara et al., 2012). According to Rahi and Malik (2016), the Romans considered edible mushrooms to be the food of the gods and included them on their list of foods to be consumed only during celebrations.Psychoactive mushrooms were mostly utilized by the Mayans for sacred ceremonies (5).Other low-digestible carbohydrates and dietary fiber are regarded as essential nutrients for human health . Numerous studies have been done on their advantages when taken as part of a food and as supplements (in isolated forms) . Reduced risk of cardiovascular disease , increased satiety, decreased postprandial blood glucose, and greater laxation are some health benefits associated with fiber ingestion. Consuming fiber may also help the gut flora, according to recent studies, especially when some fibers also act as prebiotics (6).The consumption of mushrooms has significantly expanded in recent years due to their outstanding nutritional and health benefits, which are attributed to the presence of proteins, vitamins, antioxidants, minerals, and fungal polysaccharides, particularly β-glucans.microspheres come in three varieties: glass, polymer, and ceramic. Polyethylene microspheres are frequently utilized as either temporary or permanent fillers (7). Polyethylene microspheres can form porous structures in ceramics and other materials because of their lower melting temperature. Many important nutrients and medicinal bioactive chemicals are thought to be possible to be found in mushrooms. Agaricus bisporus is the most significant commercially grown mushroom worldwide and a member of the Basidiomycetes family. This mushroom is a well-known, healthful food because of its abundance of minerals, vitamins, fiber, lipids, proteins, and carbohydrates (8). These mushrooms are known being hepatoprotective, antioxidant, antimicrobial, anticancer, antidiabetic, antihypercholesterolemic, and antihypertensive properties. They contain a number of active ingredients, including essential

amino acids, peptides, glycoproteins, polysaccharides, lipopolysaccharides, triterpenoids, nucleosides, lectins, fatty acids, and their derivatives. Reviewing contemporary research on the nutritional and therapeutic qualities of Agaricus bisporus is the main goal of this study (9).

Material – Agaricus bisporus collect from local market, Methanol,

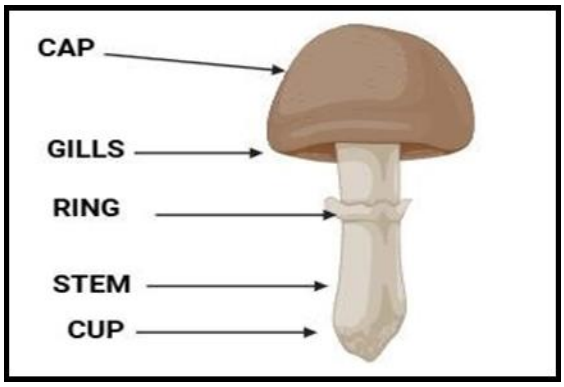


Figure 1: - Agaricus Bisporus

Phytoconstituent - Given that A. bisporus is classified as a dish that is good for people health and contains high levels of dietary fiber, antioxidants, and vitamins like thiamine, vitamin and ascorbic acid D2, in addition to minerals like folates, ergothioneine (ET), as well as polyphenol that could be beneficial for cardiovascular and diabetic conditions, it is possible that The anti-inflammatory properties of the mushroom, hypoglycemic, as well as low cholesterol properties . Together with ergosterol, tocopherols, linoleic acid, and lectins, βglucans make up around half of the bulk of the fungal cell wall (10). The primary aromatic component of mushrooms is agaritine and its derivatives, which are chemically classified as hydrazines. Certain types of mushrooms, such as A. bisporus, contain hydrazines. Agaritine has been shown to contribute to the creation of damaging aryl diazonium ions. In mushrooms, gamma-glutaminyl-4-hydroxybenzene is the main phenolic component (11).

Table 1. The components of Agaricus Bisporus

Constituent	(Unit/100 G)	References
Proximate H20	92.45 Gram	(12)
Energy	22 Kcal	(13)
Protein	93 Kj	(14)
Adjusted Protein	3.09 G	(15)
Total Lipid	2.18 G	(16)
Ash	0.34 G	(17)
Carbohydrate	0.85 G	(18)
Fiber	3.26 G	(19)
Sugar	1.98 G	(20)
Glucose	1.48 G	(1)
Fructose	0.17 G	(2)
Fiber	1 G	(3)

Table :2. The microelements that Agaricus Bisporus Contains

Microelement	Value/ (Unit/100 G)	References
Calcium (Ca)	3 mg	(4)
Iron (Fe)	0.5 mg	(5)
Magnesium (Mg)	9 mg	(6)
Phosphorus (P)	86 mg	(7)
Potassium (K)	318 mg	(8)
Sodium (Na)	5 mg	(9)
Zinc (Zn)	0.52 mg	(9)
Copper (Cu)	0.318 mg	(10)
Manganese (Mn)	0.047 mg	(11)
Selenium (Se)	9.3 µg	(12)

Material And Method for preaparation of tablet: We must take into account the following while developing an Agaricus bisporus tablet formulation that contains sustained-release antidepressant microspheres:

Agaricus bisporus: Probably utilized as a biopolymer component or functional food foundation.

Antidepressant microspheres: These are often composed of polymers like PLGA or ethyl cellulose.

Making Microspheres (per tablet basis)

- Assume that ethyl cellulose (EC) is used for prolonged release.
- The process of emulsion-solvent evaporation creates microspheres. The ratio of core to coat is 1:2 for long-term release.

Table 5.1 Ingredient for Microsphere

Sr. no.	Ingredient	Amount(mg)
1.	L lysine	10 mg per tablet
2.	Ethyl cellulose (polymer)	75 mg per tablet
3.	Ethanol (solvent)	20 ml
4.	Water	50 ml
5.	Polyvinyl alcohol (surfactant)	20 mg per tablet

Table 5.2 Ingredient for Tablet Formulation

Sr. no.	Ingredient	Qty per tablet (mg)	Qty for 30 tablets
1.	Mannitol (Bulking agent)	100	3
2.	Lactose monohydrate (Binder)	30	0.9
3.	Magnesium stearate (Lubricant)	2	0.06
4.	Silica gel (Glidant)	2	0.06

Final Steps:

- Compress into tablets using a rotary press.

Resources:

- 80g of ethyl cellulose (EC) per tablet.
- Ethanol is q.s.
- Span (as emulsifier) 80–1% w/v
- Continuous phase of distilled water.

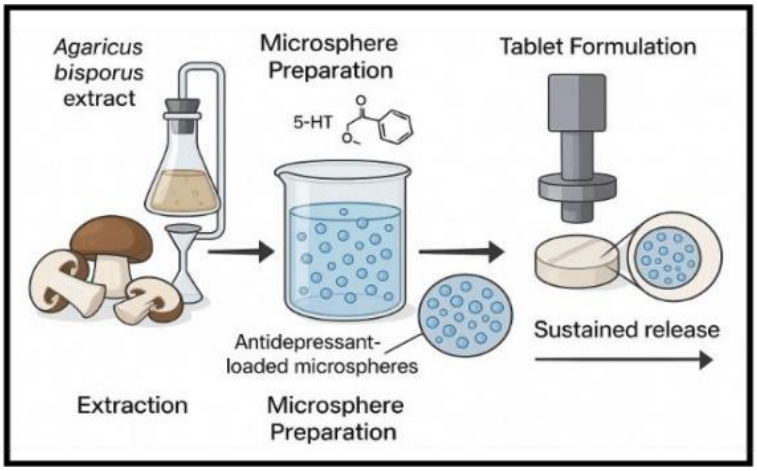


Fig.-10 Process of Tablet Formulation

Step 1: Drug-Loaded Microsphere Preparation **Method**: Evaporation of a solvent

Procedure:

1. To create the organic phase, dissolve Eudragit RS 100, Ethyl Cellulose, and Fluoxetine HCl in dichloromethane.
2. To create an oil-in-water emulsion, emulsify this organic solution into an aqueous phase using 0.5% Tween 80 while swirling rapidly.
3. Stir continuously until the solvent has completely evaporated and solid microspheres have formed.
4. The microspheres should be filtered, cleaned with distilled water, and then dried in a desiccator or under a vacuum.

Step 2: **Agaricus Bisporus extraction**

Step 3: **Mixing**

1. **Weigh and combine the following ingredients:**

a. Weight dried microsphere (120 mg), weight agaricus bisporus extract (50mg),weight HPMC(150 mg) and lactose monohydrate (0.9 mg) accurately.
b. Combine all of the weighed ingredients using petri dish
c. 10 to 15 minutes in a double-cone blender
d. Small batches are manually mixed in a clean mortar for three to five minutes using geometric dilution.
e. Make sure the excipients and active ingredients are distributed evenly.

Step 4: **Lubrication**

a. Using the overall weight of the blend, weigh the necessary amounts of magnesium stearate and talc.
b. To the previously combined combination of lactose, HPMC, Agaricus bisporus extract, and microspheres, add the lubricants.
c. To guarantee even distribution without over-lubricating, mix gently for two to three minutes with a spatula or in a suitable blender (such as a double-cone blender).
d. Before compressing, visually check the mix to make sure it is homogeneous and flows well.

Step 5: **Compression**

- Set Up the Tablet Press: Make use of a rotary tablet press that has the right dies and punches (for example, concave or flat-faced tooling, depending on the tablet design).
- Adjust machine parameters like speed and compression force.
- Feed the Blend: Fill the tablet press hopper with the lubricated powder blend. Use the appropriate feed frames or paddles to provide uniform flow and feeding into dies.

a. Modify Compression Force: To produce tablets with a target hardness of 4–8 kg/cm2, use a moderate amount of compression force.
b. To avoid shattering or harming the microspheres, which could impair sustainedrelease behavior, do not apply too much force.
c. Target Tablet Weight: 500 mg should be the approximate weight of each tablet. To ensure consistency, check the weight at regular intervals while compressing.

Step 6: **coating**

a. Resources: Ethyl cellulose or Eudragit (such as the RS/RL series) are examples of coating polymers.
b. Plasticizer: PEG 400 or triethyl citrate (optional; increases film flexibility)
c. Depending on the solubility of the polymer, the solvent can be either water, isopropyl alcohol, or a combination.

Method:

1. Get the coating solution ready.

Use the proper solvent system to dissolve the chosen polymer and plasticizer Make sure the mixture is evenly distributed and has the right viscosity for spraying.

1. Coating for Tablets:

a. Put the dried tablets in a fluid bed coater or pan coater.

b. As you rotate and apply light heat, evenly spray the coating solution onto the tablets.

c. To prevent core damage, keep an eye on the temperature (usually 30 to 40°C input air).

2. Curing & Drying:

d. Keep drying in the coater until all of the solvent has evaporated.

e. To maintain the coating, let the tablets cure (rest) at room temperature or at a little higher temperature (for example, 40°C for a few hours).

2. Completing:

Tablets can be polished with a tiny bit of talc for a nicer look.

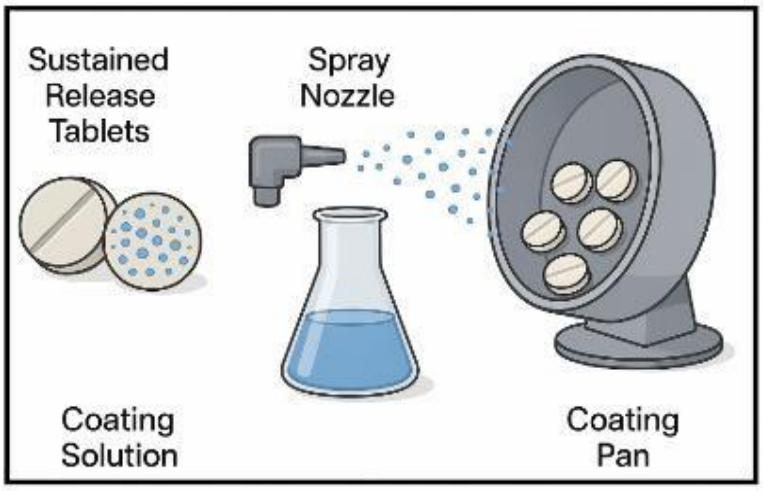


Fig.-10 Coating of Tablet

Precompression Test-

a. Particle size of microsphere -

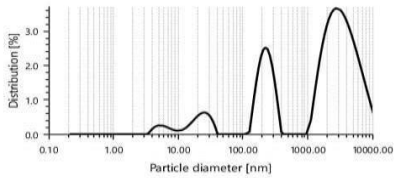
Standard Report - Particle Size

Anton Paar

Measurement information

Measurement name	Microsphere (L-Lysine)	**User**	Administrator
Method	-	**Time**	17-04-2025 17:32:14
Status	Succeeded	**Instrument type**	Litesizer 500
Measurement mode	Particle size		
Sample ID	MSLL001		
Batch number	MS/LS002		
		Filter optical density	0.501 (Automatic)
Measurement cell	Disposable	**Focus position**	0.6 mm (Automatic)
Measurement angle	Side scatter (Automatic)	**Material**	Unknown material
Target temperature	25.0 °C	**Material refractive index**	-
Equilibration time	0h 00m 10s	**Material absorption index**	-
Analysis model	General	**Solvent**	Water
Cumulant model	Advanced	**Solvent refractive index**	1.3303
Processed runs	6 (Automatic)	**Solvent viscosity**	0.0008903 Pa.s
Time for each run	0h 00m 10s (Automatic)		

Particle size distribution (intensity)



Result

Hydrodynamic diameter	949.5 nm	**Mean intensity**	169.7 kcounts/s
Polydispersity index	35.4 %	**Absolute intensity**	537.7 kcounts/s
Diffusion coefficient	0.5 µm²/s	**Intercept g1²**	0.8958
Transmittance	70.3 %	**Baseline**	2.075

Particle size distribution peaks (intensity)

Peak name	Size [nm]	Area [%]	Standard deviation [nm]
Peak 1	3778	70.40	1532.6
Peak 2	229.6	22.95	55.51
Peak 3	23.15	6.65	7.94

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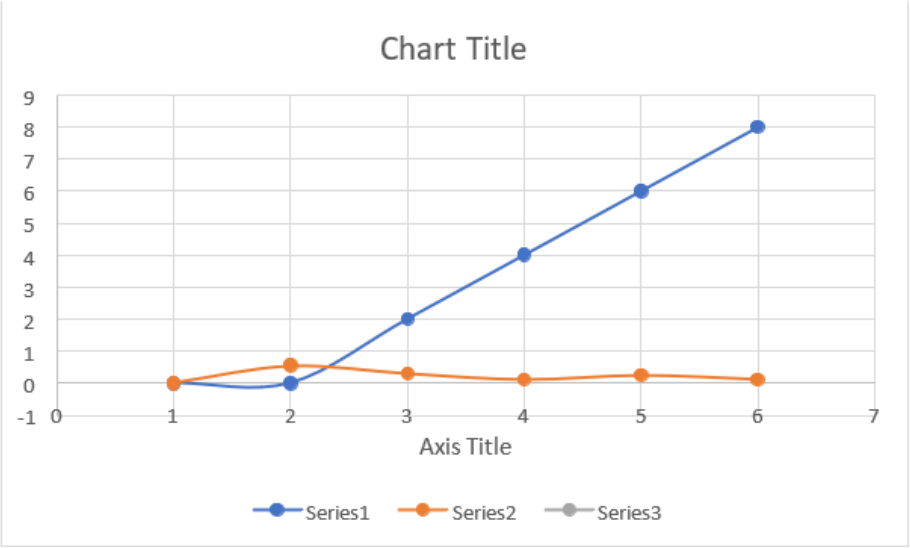
Figure No. 10 – Particle size

b. UV Spectroscopy-

Figure no.11 – UV Spectroscopy

UV graph –



1. Evaluation of Post-Compression Parameters for Tablets

- Physical attributes
- Tablet diameter and thickness
- Variation in weight
- Hardness
- Friability
- Drug uniformity and content

Post compression parameter (Tablet Evaluation)

1.Physical Appearance-

- Dimensions Shape: It is usually round or oval shape of tablet .
- Size: The diameter of tablet might vary from 6 mm to 12 mm.
- Colour: It can range from off-white to light brown and black spots are present.
- It may have a glossy or slightly tinted outer layer (such as pale yellow, white, or beige) if coated for prolonged release.
- Texture of the Surface: consistent and smooth if film-coated.If uncoated, it could be a little rough or speckled with visible mushroom material.

2. Tablet diameter and thickness – 8 to 12 mm 8 mm is typical for smaller dosages. For sustained-release formulations that need more excipients or microspheres, 10–12 mm is the norm.

Tablet Density: 3 to 6 mmThe volume of the microspheres and matrix materials, as well as the compression force, determine thickness.

Variation of weight-

a. Choose 20 tablets at random from the batch.
b. Use an analytical balance to weigh each tablet separately, then note the weights.
c. Determine the ten tablets' average weight.
d. Using the formula below, determine each tablet's percentage variation from the average weight.
e. Examine the differences in relation to the official USP limits.

Observation table:

Sr. No.	Weight (mg)

1	510
2	512
3	509
4	508
5	513
6	507
7	514
8	505
9	511
10	506

Calculation:

1. Average weight: sum of all tablet weight

Average weight = $\frac{5095}{10} = 509.5$

2. Calculate Deviation for each tablet

Deviation from average weight:

$$\textit{Initial weight of tablet} - \textit{average weight of tablet}$$

Percentage deviation $\left(\frac{\textit{Initial weight of tablet} - \textit{average weight of tablet}}{\textit{average weight of tablet}}\right) x100$

% Deviation Average= $\left(\frac{\textit{Initial weight of tablet} - \textit{average weight of tablet}}{\textit{average weight of tablet}}\right) x100$ = % deviation

1.**Final Conclusion**

- Average Weight = 508.7
- All 20 Tablet Are Within $\pm$ 5% of average weight

2.**Hardness:**

Tools: Tablet Hardness Tester (e.g., Pfizer, Monsanto, or digital testers such as Schleuniger or Erweka) Scale that has been calibrated (for weight reference)

The size of the sample

To guarantee consistency, ten pills are usually tested.

Approach for Hardness tester:

1. Set the hardness tester's calibration.
2. Insert each tablet into the gadget separately.
3. Continue applying pressure until the tablet shatters.
4. Note the force (in kp or N) at which each tablet breaks.
5. Repeat for all 10 tablets.

Hardness testing by Monsanto apparatus:

- A manual tool for determining a tablet's crushing strength (hardness) is the
- Monsanto hardness tester. The steps to use the Monsanto tester are as follows:
- Procedure: for the Monsanto Hardness Tester using a spring mechanism, the tester applies a compressive force diametrically across the tablet until it breaks. The necessary force is expressed in Newtons or kg/cm².

Supplies Needed:

- Hardness tester made by Monsanto Test tablets (typically six on average)
- Cleaning cloth or tissue

Method

- Make sure the device is calibrated by using a recognized tablet or a standard weight.
- Getting ready Check that the scale and plunger are free to move by eaning the tester.If necessary, adjust the zero scale.

- Position the tablet The tester should be held vertically.
- Align one tablet diametrically (flat surface against the plungers) between the tester's two jaws, or anvils.
- To raise the pressure, slowly turn the screw knob on the tester's end.
- Until the pill breaks, keep applying pressure.
- Take note of the reading that causes the tablet to shatter. This is the hardness value, usually expressed in Newtons (N) or kg/cm².

Friability: To assess the tablets' resistance to mechanical shock or abrasion during handling, packing, and transit.

Procedure:

Weighing

- Choose ten to twenty tablets and weigh them precisely.
- Note the starting weight (W_0).

2. Examination:

- Put the tablets in the friabilator drum.
- At 25 rpm, rotate the drum 100 times, which takes around 4 minutes.

Calculation:

Initial weight total (w_0) = 10000

Final total weight (w_1) = 9820

$$\text{Friability} = \left(\frac{W0\ \textbf{initial weight} - W1\ FINALweight}{W0 initial\ weight}\right) x100$$

$$= \left(\frac{10000 - 9820}{10000}\right) x100$$

$$= 0.018\ x100 = 1.8\%$$

Friability is 1.8% pass the friability.

Disintegration time: To ascertain, under controlled circumstances, the rate at which a tablet disintegrates into smaller pieces in a certain liquid media.

Equipment:

- Disintegration Test Equipment (in accordance with USP, BP, and IP standards)
- Beaker or one-liter container
- A water bath with a thermostat (to maintain 37 ± 2°C)
- Basket rack assembly disintegration
- Distilled water or a designated medium (phosphate buffer, 0.1N HCl, etc.)

Conditions of the Test:

- 37 ± 2°C is the medium temperature.
- There are six pills.
- 900 mL is the medium volume.
- Movement of the basket: about 30 cycles per minute (up and down)

Method:

1. Fill each tube of the disintegration basket with one of the six tablets.
2. Place a disc over each tablet, if necessary.
3. Hang the basket in the test medium-filled disintegration equipment.
4. Turn on the device and note how long it takes for each tablet to dissolve completely.

Acceptance Criteria (USP/BP/IP):

- Uncoated tablets: Must disintegrate within 15 minutes
- Film-coated tablets: Must disintegrate within 30 minutes

S. No.	Tablet no.	Start time	End time	Disintegration time(min:sec)
1	1	0	25:20	25:20
2	2	0	26:30	26:30
3	3	0	24:30	24:30
4	4	0	28:05	28:05
5	5	0	28:30	28:30
6	6	0	24:00	24:00

Conclusion: All 6tablet disintegrated within 30min.

3. **Sustained-release**: The medication should be released by the formulation over a period of 12 to 24 hours.

6.1 RESULT AND DISCUSSION OF FORMULATION: -

Behavioral Testing On Mice- When compared to the control group, mice given 200 mg/kg of A. bisporus extract for 14 days shown a substantial decrease in immobility time in the Forced Swim Test (FST) and Tail Suspension Test (TST) ($p < 0.05$). These behavioral results are similar to those seen with fluoxetine, a common antidepressant, indicating possible effects similar to those of antidepressants.

Literature Review Findings: There is a statistically significant negative relationship between the risk of depression and mushroom consumption, according to observational research (such as those from the National Health and Nutrition Examination Survey, or NHANES). According to a large cohort research, regular mushroom users were 43% less likely to suffer from depression than non-users.

Microsphere Formulation and Characterization:

Using ethyl cellulose (EC) as a sustained-release polymer, the solvent evaporation method was effectively used to create Agaricus bisporus extract microspheres.

Parameter Observation Size (µm) 210 ± 15

Yield (%) 85.3 ± 2.1

Efficiency of encapsulation (%) 78.6 ± 3.2

Percentage of drugs loaded (24.7 ± 1.8)

The microspheres' smooth surfaces and spherical shape.

Drug Release in Vitro

Agaricus bisporus extract was released continuously over a 12-hour period, with a cumulative release of 68%, according to the in vitro release research.

Assessment of Tablets

Tablets based on microspheres were crushed and assessed:

Parameter	Result
Hardness	5.2 ± 0.4 kg/cm²
Friability (%)	0.42 ± 0.1
Disintegration Time	> 60 minutes (sustained type)
Weight variation	Within pharmacopeial limits

CONCLUSION -Because of its high nutritional content, a bisporus may offer substantial protection against malnutrition, particularly in

developing and underdeveloped nations. Although A. bisporus has medicinal properties, especially as an antioxidant, antibacterial, anticancer, and anti-cardiovascular disease agent, however it is not good for your diet. In recent decades, edible mushrooms have gained popularity as a source of medication or as an addition to health foods. This adage is appropriate for mushrooms because of their amazing therapeutic food, medicine, and mineral properties. They are therefore a great advantage for human welfare. In the future, A. bisporus may be employed to treat a variety of illnesses and serve as a vital component or backbone of research.

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