ADVANCED PENETRATION TECHNOLOGY

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Drug Resistant *Candida auris*: The "Nearly Perfect Pathogen" Emerging Global Healthcare Threat

Advanced Penetration Technology, LLC (APT, LLC), is an Indiana and Texas based company.

Founded in in 2016, APT, LLC strives to provide access to highly effective care at the primary and consumer healthcare levels on a global scale.

APT, LLC is a **pharmaceutical intellectual property (IP) company** that has created new solutions that use APT™ based products targeting wounds, resistant bacterial and fungal infections.

Advanced Penetration Technology (APT™)

- APT™ is a novel, proprietary (patent pending) topical transdermal carrier platform formulation.

- APT™ imparts a unique biophysical and biochemical action which has proven highly effective in killing bacteria, fungus and neutralizing viruses. Effective against resistant microbes.

- APT™ has broad utility to enhance the activity of a wide spectrum of active pharmaceutical ingredients (API's) .

APT™ Formulation to Combat Multi-Drug Resistant *Candida auris*: Emerging Global Healthcare Threat

Candida auris is a multi-drug resistant fungus which can be fatal, particularly if it enters the bloodstream of the patient. These infections are associated with high mortality rates.

Skin colonization by *C. auris* in hospitalized patients acts as a nidus of infection. Unfortunately current approaches to decolonize the skin are ineffective.

APT™ **preventative focus** for *C. auris*: Aim is to develop a skin decolonizing formulation to be used by patient and healthcare workers to stop the spread of infection due to this multi-drug resistant pathogen.

APT™ possesses potent anti- *C. auris* "in vitro" activity

- **Minimum Inhibitory concentration of 1% Terbinafine Transdermal Dual Carrier Platform, (TDDC) and fluconazole was determined using CLSI- M27 methodology.**

- **CONCLUSION:** The data show that 1% TDDC possesses a potent antifungal activity against *C. auris* that are susceptible and resistant to fluconazole.

Appendix

Raw Data

MRL #	Isolate	TDDC (µg/mL)	Fluconazole (µg/mL)
35645	*C. auris*	2.4	1
35646	*C. auris*	1.2	1
35647	*C. auris*	0.6	64
35648	*C. auris*	1.2	64
35649	*C. auris*	4.9	>64
35650	*C. auris*	4.9	>64
35651	*C. auris*	4.9	1
35652	*C. auris*	1.2	>64
35653	*C. auris*	2.4	>64
35654	*C. auris*	2.4	>64
39414	*C. auris*	1.2	1
39415	*C. auris*	0.6	8
39416	*C. auris*	0.6	>64
39417	*C. auris*	0.6	>64
39418	*C. auris*	2.4	16
39419	*C. auris*	1.2	32

APT™ Formulations are effective against Terbinafine Resistant *C. auris* in vitro.

- APT™ Formulations [Terbinafine 1% and APT™ Clotrimazole 1%] were evaluated against Terbinafine Resistant Strains of *C. auris (n=8)* provided by the CDC in vitro

CONCLUSION: APT™ Formulations demonstrated potent antifungal efficacy against these resistant strains compared to a terbinafine API.

Table 1. MIC values (µg/mL) for 1% Terbinafine, 1% Clotrimazole and the terbinafine control against the terbinafine resistant *C. auris* isolates tested (n=8).

Strain	CDC #	Terbinafine Control	1% Terbinafine		1% Clotrimazole	
			MIC	Fold decrease[a]	MIC	Fold decrease
C. auris	B11103	2	1.2	1.7	0.3	6.7
C. auris	B11221	8	0.6	13[b]	≤0.01	800[b]
C. auris	B11227	2	1.2	1.7	≤0.01	200[b]
C. auris	B11228	4	0.04	100[b]	≤0.01	400[b]
C. auris	B11799	>64	1.2	53[b]	0.08	800[b]
C. auris	B11808	>64	0.08	800[b]	1.2	53[b]
C. auris	B11809	32	0.08	400[b]	0.3	106[b]
C. auris	B12135	>64	0.3	213[b]	0.3	213[b]
	MIC Range	**1->64**	**0.08-1.2**		**≤0.01-1.2**	

[a]Decrease in MIC values when compared to the terbinafine control.
[b]An significant decrease in MIC value when compared to the terbinafine control.

APT™ Formulations are effective against Terbinafine Resistant *C. auris* in vivo.

- Two APT™Formulations [Terbinafine 1% & Clotrimazole 1%] Mouse Skin Decolonization Study - **Development of a *Candida auris* skin colonization murine model to evaluate the antifungal efficacy of 1% Terbinafine Transdermal Dual Carrier Platform (TTDCP) and 1 % Clotrimazole Transdermal Dual Carrier Platform (CTDCP)**

CONCLUSION: 1% Terbinafine Transdermal Dual Carrier Platform (TTDCP) and 1% Clotrimazole Transdermal Dual Carrier Platform (CTDCP) demonstrated potent antifungal efficacy against *C. auris* in a murine model of skin colonization. The data suggests that 1% TTDCP and 1% CTDCP is effective as a skin decolonizer.

Table 1. Right ear tissue fungal burden with *P*-values when compared to the untreated control

	Average Log CFU/g ± SD	*P*-value vs. Untreated
Untreated	7.79 ± 0.1	-------
Vehicle	7.58 ± 0.1	0.0353
1% TTDCP	4.59 ± 0.1	< 0.0001
1% CTDCP	4.43 ± 0.1	< 0.0001

Table 2. Left ear tissue fungal burden with *P*-values when compared to the untreated control

	Average Log CFUs ± SD	*P*-value vs. Untreated
Untreated	7.72 ± 0.1	-------
Vehicle	7.76 ± 0.1	0.9422
1% TTDCP	4.40 ± 0.1	< 0.0001
1% CTDCP	4.36 ± 0.1	< 0.0001

Table 3. Back tissue fungal burden with *P*-values when compared to the untreated control

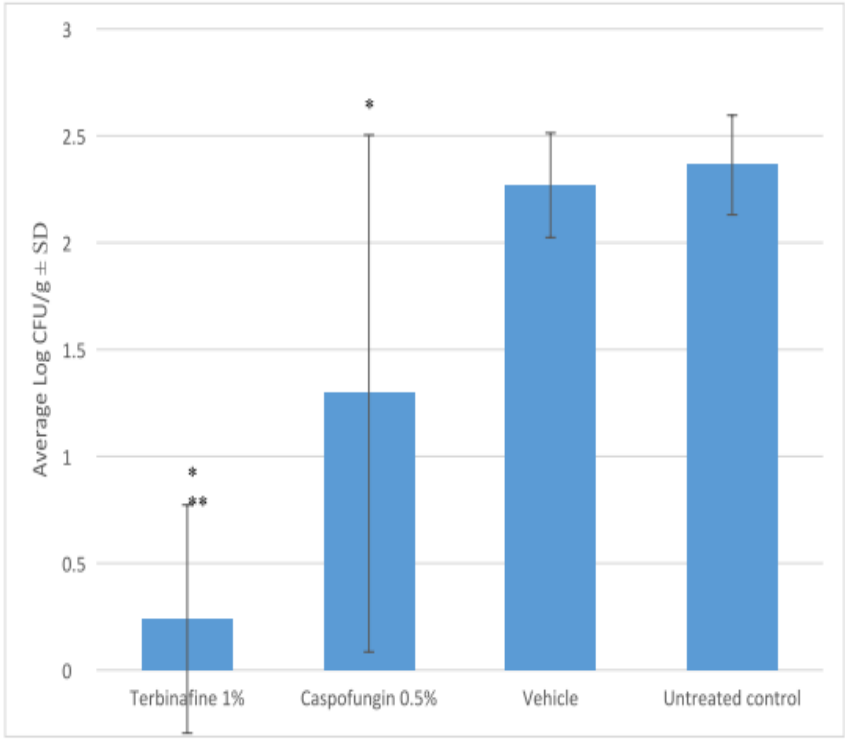
	Average Log CFUs ± SD	*P*-value vs. Untreated
Untreated	7.33 ± 0.2	-------
Vehicle	7.66 ± 0.2	0.1003
1% TTDCP	4.29 ±0.2	< 0.0001
1% CTDCP	4.51 ± 0.1	< 0.0001

APT™ Formulation is effective against *C. auris* wound infection model.

- APT™ Antifungal *Candida auris* Wound study – **Evaluate the antifungal efficacy of a Novel 1% Terbinafine Transdermal Dual Carrier Platform (TTDCP) against *C. auris* using a guinea pig model of cutaneous infection.**

CONCLUSION: Treatment with the novel APT™ 1% Terbinafine formulation reduced the fungal burden in skin challenged with *C. auris* when compared to the untreated control.

Figure 1. Tissue fungal burden of infected skin.



*Statistically significant difference when compared to the untreated control.
** Statistically significant difference when compared to the vehicle control.

- “Using a *C. auris* decolonization model we were able to demonstrate that treatment with APT was effective in decolonizing the skin of this multidrug resistant yeast. These findings suggest this topical formulation may provide a safe and easy method to decolonize the skin of both healthcare workers and patients thereby interrupting skin colonization by the dangerous pathogen, *Candida auris”.*

  Mahmoud Ghannoum, PhD Case Western Reserve University

  Professor, Department of Dermatology, School of Medicine

  Professor, Department of Pathology, School of Medicine

  Fellow of the American Microbiology Society

  Peer Reviewed Published Manuscript: Antimicrobial Agents and Chemotherapy 2021

  https://pubmed.ncbi.nlm.nih.gov/33558297/

PFTH, LLC Objective

Patient Focused Telehealth, LLC (parent company), is a Texas/Indiana based intellectual property development company seeking to License the APT™ formulation intellectual property (IP). We are seeking strategic partnerships with governmental and/or Industry leaders for the production and distribution of APT™ formulations and future APT™ platform-based product development.

APT™ Based Formulations

APTT3X™ / APT™- Tetracycline 3% - broad spectrum antibiotic

APT™-Terbinafine 1% - antifungal

APT™-Clotrimazole 1% - antifungal

T3 Wound Wash™ – broad spectrum antibacterial wound cleanser.

Arthro Care™ – topical pain relief medication for arthritis, muscle, tendon, neck and back.

CALM Recovery™ – topical inflammation, swelling and bruising relief for aesthetic procedures.