Received: 9 September 2020 | Revised: 2 January 2021 | Accepted: 7 March 2021

DOI: 10.1111/dth.14935

SHORT PAPER

DERMATOLOGIC THERAPY WILEY

Chitin-lipid interactions and the potential relationship between Demodex and SARS-CoV-2

Alin Laurentiu Tatu[1,2] | Thomas Nadasdy[1] | Lawrence Chukwudi Nwabudike[3]

[1]Dermatology Department, "St. Parascheva" Clinical Hospital of Infectious Diseases, Galati, Romania

[2]Faculty of Medicine and Pharmacy/Clinical Department, Dermatology, Medical and Pharmaceutical Research Unit/Competitive, Interdisciplinary Research Integrated Platform, ReForm-UDJG, Dunărea de Jos" University, Galati, Romania

[3]N. Paulescu National Institute of Diabetes, Bucharest, Romania

Correspondence
Thomas Nadasdy, Dermatology Department, "St. Parascheva" Clinical Hospital of Infectious Disease, Str. Varful cu Dor 23/3, Arad, AR, Romania.
Email: thomas.nadasdy@gmail.com

Abstract

Already from the early days of the COVID-19 pandemic, regulatory agencies have attempted to ascertain the possible routes of SARS-CoV-2 viral transmission. It is hypothesized that the lipid bilayer that surrounds the SARS-CoV-2 improves its ability to remain stable on sebum-rich skin and serves as another possible route of contracting the virus. One possible aspect of these observations that has yet to be explored in detail is what role arthropods that have been associated with human skin infestation, such as *Demodecidae* or *Pyemotidae* species, play in viral transmission. It seems likely that arthropod-coronavirus interactions may take place through the molecular attraction forces between the chitin found on the exoskeleton of mites commonly found on human skin and the lipids present on the viral envelope of the SARS-CoV-2. We believe this may mean that arthropods are currently an overlooked cofactor in viral infection which may have some important biomedical implications for both prevention and treatment.

KEYWORDS
chitin, Demodex, SARS-CoV-2

Already from the early days of the COVID-19 pandemic, regulatory agencies have attempted to ascertain the possible routes of SARS-CoV-2 viral transmission. While person-to-person transmission via respiratory droplets is currently considered by both the World Health Organization and Centers for Disease Control and Prevention as the primary manner through which SARS-CoV-2 spreads, other authors have also made a case for transmission via the gastrointestinal tract, sexual contact and contact with viral particles found on surfaces and other fomites. The latter of which appears to be backed by a study demonstrating viral stability ranging from 72 hours on plastic surfaces to 4 hours on copper.[1] Recent reports have also shown that the SARS-CoV-2 may also be transmitted via close contact, even clustering within families.[2,3] Sexual contact has been linked to coronavirus transmission not only through accelerated breathing, but also with the potential for alternative forms of transmission such as through oroanal contact, skin-to-skin contact, or contact with COVID-19-related skin manifestations, such as COVID vesicles or other COVID rashes.[4,5] It is hypothesized that the lipid bilayer that surrounds the SARS-CoV-2 improves its ability to remain stable on sebum-rich skin and serves as another possible route of contracting the virus. Indeed, coronaviruses are known to make use of lipids as target cell entry receptors, and as factors in viral replication complex synthesis and formation. Moreover, a recent study showed that small molecules such as sterols and cyclodextrin may disrupt the lipid-dependent attachment of the virus to host cells, and as such may reduce the infectivity of the SARS-CoV-2.[6] One possible aspect of these observations that has yet to be explored in detail is what role arthropods that have been associated with human skin infestation, such as *Demodecidae* or *Pyemotidae* species, play in viral transmission. These arthropods share a common polymer, chitin, as an integral part of their exoskeletons. Chitin and chitosan, the enzymatic product of chitin produced through bacterial degradation, have unique properties that have stimulated interest in their possible biomedical applications. They are both non-toxic, biodegradable, biocompatible, and can form films on the skin, and these unique properties have allowed chitin to be employed to act as a scaffold for the building of nanoparticles to enhance drug delivery for topical application.[7] It is precisely their biochemical characteristics that might also permit them to interact with lipid molecules found on the surface of

viral particles. The authors have demonstrated attraction between chitosan molecules and those of fatty acids through electrostatic and hydrophobic forces, along with hydrogen bonding occurring between the two.[8] Wydro et al demonstrated the interactions of chitosan with both saturated and unsaturated fatty acids by creating Langmuir films of selected lipids on an acetate buffer that contained varying concentrations of chitosan. The presence of chitosan in the buffer influenced the size and location of the lipid deposition, and monolayer expansions were observed with all lipids tested roughly proportional to the concentration of chitosan present in the buffer. It was also noted that the compactness of the lipid monofilms was modified for each lipid tested in the presence of chitosan saturation. The solid monolayers of stearic acid and cholesterol were loosened, whereas the liquid monolayers of the unsaturated acids were tightened.[9] Most of the naturally occurring polysaccharides, such as cellulose, dextran, pectin, alginic acid, agar, agarose, and carrageenan are either neutral or acidic in nature, whereas chitosan is an example of a highly basic polysaccharide. Other unique properties of chitin and chitosan include their ability to form polyoxysalts, their ability to form films, their biocompatibility, biodegradability, and non-toxicity, along with their unique molecular adsorption properties.[7]

Lipids are key players during viral infection, as they are necessary for viral membrane fusion to that of host cells, viral replication, and viral exocytosis and endocytosis. They act either directly or indirectly as receptors for viral entry, or as cofactors that allow for viral fusion or entry into targeted host cells. Once a host cell is infected, viruses can hijack host cell lipid signaling and synthesis pathways to induce the production of lipids for their own envelopes. Finally, lipids are also known for their roles in viral envelopment and transformation, and molecules that target lipids such as cholesterol and sphingolipids might be used to selectively block viral replication. Keeping this in mind, we propose that through its chitin exoskeleton, *Demodex folliculorum* may act as a reservoir that binds SARS-CoV-2 viral particles allowing them to remain stable on the surface of the skin for a longer duration, and therefore might represent an overlooked cofactor in viral transmission, especially in those who are already in close contact. This raises the question of whether behavioral modifications in those who share close-quarters may play a role in viral transmission. Suggested behavioral changes such as cutting nails short, keeping hair tied back, shaving beards, avoiding eyelash extensions, disinfecting personal hygiene tools, and maybe even sexual abstinence have all been proposed in an attempt to limit SARS-CoV-2 spread.[3] Surveyed females queried on recent sexual behavioral changes in relation to the COVID-19 pandemic have reported feelings of anxiety, fear, frustration, lack of sexual interest, and decreased desire to become pregnant. This is also in line with reports of lowered demands for sexually transmitted disease outpatient services.[8,10,11] However, it is possible that close skin-to-skin contact especially in seborrheic areas, either within families or via sexual contact, may be another route through which SARS-CoV-2 transmission may occur, and that such transmission may be enhanced by the presence of *D. folliculorum*.

Another perspective on the relationship between *D. folliculorum* and the SARS-CoV-2, as some authors have suggested, would be to potentiate a topical RNA vaccine containing lipid nanoparticles that may stimulate dendritic cells directly within the skin, which could in turn induce a systemic immune response. The mites, who embed themselves inside pilosebaceous follicles to feed on the lipid-rich sebum, could potentially be harvested and used as carriers to transport vaccine antigens directly into pilosebaceous units where they would exert a more powerful source of antigenic stimulation. The resulting antibodies against the mites could then be reproduced and formulated as antibody-vaccine complexes for topical administration.[12] Antigenic stimulation via topical vaccines may be used to potentiate parenteral vaccines, or they may prove useful in a similar manner as oral polio vaccines by producing a local IgA immune response that offers further protection than that which can be offered by classic parenteral vaccination. While it is true that the oral polio vaccine stimulates a response locally at the site of polio infection in the gut, and COVID-19 is primarily a respiratory virus, this proposed method could perhaps elicit an IgA response that would destabilize viral particles present on mucocutaneous surfaces which would complement the protection it offers through systemic immune induction. Topical vaccines may also be cheaper to produce, and they may be more stable at elevated temperatures, therefore allowing greater use in underdeveloped areas incapable of providing a proper cold-chain necessary for parenteral vaccines. This form of vaccination and its mode of administration may also be more attractive to those who oppose vaccination for various reasons, including fear of autism from vaccine contents such as aluminum, as the mites naturally grow on human skin.

It seems likely that arthropod-coronavirus interactions may take place through the molecular attraction forces between the chitin found on the exoskeleton of mites commonly found on human skin and the lipids present on the viral envelope of the SARS-CoV-2. We believe this may mean that arthropods are currently an overlooked cofactor in viral infection which may have some important biomedical implications for both prevention and treatment.

CONFLICT OF INTEREST

The authors declare no potential conflict of interest.

DATA AVAILABILITY STATEMENT

Data sharing not applicable to this article as no datasets were generated or analyzed during the current study.

ORCID

Alin Laurentiu Tatu https://orcid.org/0000-0003-4290-7068
Thomas Nadasdy https://orcid.org/0000-0002-1196-8100
Lawrence Chukwudi Nwabudike https://orcid.org/0000-0003-0774-7396

REFERENCES

1. Van Doremalen N, Bushmaker T, Morris DH, et al. Aerosol and surface stability of SARS-CoV-2 as compared with SARS-CoV-1. *N Engl J Med*. 2020;382:1564-1567. https://doi.org/10.1056/NEJMc2004973.

2. Tatu AL, Nadasdy T, Bujoreanu FC. Familial clustering of COVID-19 skin manifestations. *Dermatol Ther*. 2020;14:e14181. https://doi.org/10.1111/dth.14181.
3. Tatu AL, Nadasdy T, Nwabudike LC. Observations about sexual and other routes of SARS-CoV-2 transmission and its prevention. *Clin Exp Dermatol*. 2020;45(6):761-762. https://doi.org/10.1111/ced.14274.
4. Tatu AL, Kluger N, Nwabudike LC. Pain and shingles on an old scar. *Int J Dermatol*. 2020;59(9):1158-1159. https://doi.org/10.1111/ijd.15046.
5. Wollina U, Karadağ AS, Rowland-Payne C, Chiriac A, Lotti T. Cutaneous signs in COVID-19 patients: a review. *Dermatol Ther*. 2020;33(5):e13549. https://doi.org/10.1111/dth.13549.
6. Baglivo M, Baronio M, Natalini G, et al. Natural small molecules as inhibitors of coronavirus lipid-dependent attachment to host cells: a possible strategy for reducing SARS-COV-2 infectivity? *Acta Biomed*. 2020;91(1):161-164. https://doi.org/10.23750/abm.v91i1.9402.
7. Elieh-Ali-Komi D, Hamblin MR. Chitin and chitosan: production and application of versatile biomedical nanomaterials. *Int J Adv Res (Indore)*. 2016;4(3):411-427.
8. Nadasdy T, Clatici VG, Barinova E, Tatu AL. Comments on "does COVID-19 influence sexual behaviours?". *Dermatol Ther*. 2020;33(6):e14083. https://doi.org/10.1111/dth.14083.
9. Wydro P, Krajewska B, Hąc-Wydro K. Chitosan as a lipid binder: a Langmuir monolayer study of chitosan–lipid interactions. *Biomacromolecules*. 2007;8:2611-2617. https://doi.org/10.1021/bm700453x.
10. Gaspari V, Orioni G, Viviani F, Raone B, Lanzoni A, Bardazzi F. Does COVID-19 influence sexual behaviors? *Dermatol Ther*. 2020;33(6):e14004. https://doi.org/10.1111/dth.14004.
11. Tatu AL, Nadasdy T, Nwabudike LC. New data about sexually transmitted COVID19. *Dermatol Ther*. 2020;30(6):e14426. https://doi.org/10.1111/dth.14426.
12. Strobel SL. Could Demodex be used to augment a topical vaccine against coronavirus (and similar viruses)? *Ann Clin Lab Sci*. 2020;50(3):314-315.

How to cite this article: Tatu AL, Nadasdy T, Nwabudike LC. Chitin-lipid interactions and the potential relationship between Demodex and SARS-CoV-2. *Dermatologic Therapy*. 2021;34:e14935. https://doi.org/10.1111/dth.14935