Journal of Research in Medical and Dental Science
2020, Volume 8, Issue 4, Page No: 107-109

Available Online at: www.jrmds.in
eISSN No. 2347-2367: pISSN No. 2347-2545

Infertility: Plant Derived Bitter Tasting Compounds to Slack off the Bitterness of Genital Infections. Real or Just a Hype?

Menizibeya O Welcome*, Senol Dane

Department of Physiology, Faculty of Basic Medical Sciences, College of Health Sciences, Nile University of Nigeria, Abuja, Nigeria

HOW TO CITE THIS ARTICLE: Menizibeya O Welcome, Senol Dane, Infertility: Plant Derived Bitter Tasting Compounds to Slack off the Bitterness of Genital Infections. Real or Just a Hype? J Res Med Dent Sci, 2020, 8 (4):107-109.

Corresponding author: Menizibeya O Welcome

e-mail✉: welcome.menizibeya@nileuniversity.edu.ng

Received: 01/07/2020

Accepted: 20/07/2020

LETTER TO EDITOR

Infertility refers to the inability of a reproductive-aged woman (from 15 to 49 years old) to conceive after 12 months of sexually active life [1]. Globally, infertility affects about 80 million couples and is associated a huge psychosocial burden [2]. Both male and female factors comprising about 20–50% and 26-50% respectively contribute to development of infertility. Though multiple causes of infertility have been reported [3–5], genital infections continue to constitute the greatest risk for infertility, accounting for about 15–35% of infertility cases in males [5] and 50–75% of infertility cases in females [4]. Despite substantial improvement in medical treatment, incidence of genital infections has continued to increase over the past years in addition to ever increasing microbial resistance experienced in clinical practice [1,5]. This evidently substantiates the need to search for alternative areas that may lead to discovery of novel therapy for genital infections.

Bitter taste receptors (T2Rs) were initially discovered in the gastrointestinal tract, and are now believed to be expressed in many regions of the body where they detect toxins to mobilize protective mechanisms that ensure elimination of the toxins, and also, serve as sentinels of the immune system [6]. Relatively recently, T2Rs were found in cell and tissues of the cervix, vagina, endometrium, myometrium, placenta, ovary, prostate, testis, and spermatozoa [7–9]. T2Rs are transmembrane G protein-coupled receptors (GPCR) that sense bitter compounds by stimulating the α-gustducin, which signals downstream the cell, activating cytoplasmic acceptors that mediate responses that subsequently culminate in activation of defense mechanisms aimed at abating pathogenic aggression [7, 8]. To date, twenty-five human T2Rs have been discovered and are activated by bitter molecules including caffeine, amarogentin, denatonium, among others. There are more than 1000 currently identified bitter compounds [10] and numerous naturally occurring bitter compounds mainly derived from plant sources [11]. The following plant derived bitter tasting compounds are potential activators of T2Rs: (-)-epicatechin, (−)-epigallocatechin gallate, 6-n-propyl-2-thiouracil, 8,8'-bieckol, amarogentin, andrographolide, anthocyanin, apigenin, apocynin, arctigenin, berberine, caffeic acid, catechin, chlorogenic acid, clovamide, crebanine, cryptolepine, cryptopleurine, cyanidin, dicentrine, dieckol, diphenitol, eckol, ellagic acid, ferulic acid, fisetin, gallic acid, isoliquiritigenin, isoorientin, isorhynchophylline, kaempferol, kolaviron, leonurine, neoechinulin A, nobiletin, O-methylbulbocapnine, oxymatrine, paeonol, procyanidin A2, protocatechuic acid, pseudocoptisin, punicalagin, quercetin, quinine, resveratrol, rhynchophylline, sinomenine, skimmianine, tangeretin, tetrandrine, theaflavins, tournefolic acid B, tryptanthrin, umbelliferone, xanthoxin, and yohimbine [11]. Though is lack of studies, these polyphenols, tannins, anthocyanins, alkaloids, and quinolones are natural chemicals that can be harnessed as

T2R agonists for possible future therapeutics of genital infections.

Binding of the bitter compounds to T2Rs causes stimulation of the α-gustducin, which signals downstream intracellular proteins that ultimately culminates in activation of inflammatory signaling cascades that appear to serve as defensive mechanisms against the pathogens [12]. Though the molecular pathways are not exactly known, available evidences [12–14] suggest that defensive mechanisms against the pathogens due to activation of T2Rs by their agonists (i.e. bitter compounds) is associated with inflammatory signaling cascades that appear to be associated with the master regulators of inflammation –NF-κB (nuclear factor kappa-light-chain-enhancer of activated B cells) and NLRP3 (nucleotide-binding oligomerization domain, leucine rich repeat and pyrin domain containing 3) inflammasome. NF-κB is transcription factor that control gene expression of NLRP3 and proinflammatory cytokines/ chemokines. The NLRP3 inflammasome is a key inflammatory molecule in priming and maturation of inflammatory cytokines. Under normal conditions, the NF-κB and NLRP3 are controlled at low level and inactive in cells through specific molecular interactions that prevent their activation. However, in cases of T2R dysfunctions, activation of NF-κB and NLRP3 inflammasome cascades and the resultant upstream signaling may stimulate the matrix metallopeptidases or other proteolytic enzymes to mediate characteristic inflammatory and destructive processes in cells and tissues of the genital tract.

Indeed, dysfunctional T2R signaling in spermatozoa was demonstrated to cause multiple damages by microbial pathogens, suggesting that disorders in genital tract T2R signaling may predispose or even cause genital infections, which in turn may lead to infertility [15]. Similar findings were reported by Deckmann et al. who demonstrated T2Rs of the urogenital tract effectively detected bitter substances and uropathogenic Escherichia coli to initiate cellular signaling that ultimately resulted in prevention of pathogenic colonization of the tract [16]. Zheng et al. also reported that chloroquine, a T2R agonist, prevented uterine infection induced by bacterial lipopolysaccharide in experimental animals through activation of the α-gustducin [8]. Interestingly, this protective effect of chloroquie was abolished in α-gustducin knock out animals [8].

It is therefore important for future studies to investigate the role of T2R signaling and bitter tasting compounds derived from different plant sources in genital tract infections, and possibly on animal models of infection-induced fertility. It is not also known how these T2Rs may affect endocrine functions of the gonads. Thus, goal driven research aimed at unraveling the relationship between T2R signaling and endocrine functions of the gonads may provide further insights into potential molecular culprits of infertility.

REFERENCES

1. World Health Organization. Reproductive health indicators for global monitoring: Report of the second interagency meeting. Geneva: World Health Organization 2001.
2. Mascarenhas MN, Flaxman SR, Boerma T, et al. National, regional, and global trends in infertility prevalence since 1990: A systematic analysis of 277 health surveys. PLoS Med 2012; 9:e1001356.
3. Briceag I, Costache A, Purcarea VL, et al. Fallopian tubes–literature review of anatomy and etiology in female infertility. J Med Life 2015; 8:129–131.
4. Dalal R. Infection and infertility, genital infections, and infertility. Edn. Darwish AM. In: Genital infections and infertility. Rijeka, Croatia: Intech Open 2016; 3–19.
5. Solomon M, Henkel R. Semen culture and the assessment of genitourinary tract infections. Indian J Urol 2017; 33:188-193.
6. Welcome MO, Mastorakis NE, Pereverzev VA. Sweet taste receptor signaling network: Possible implication for cognitive functioning. Neurol Res Int 2015; 2015:606479.
7. Xu J, Cao J, Iguchi N, et al. Functional characterization of bitter-taste receptors expressed in mammalian testis. Mol Hum Reprod 2013; 19:17–28.
8. Zheng K, Lu P, Delpapa E, et al. Bitter taste receptors as targets for tocolytics in preterm labor therapy. FASEB J 2017; 31:4037-4052.
9. Wölfle U, Elsholz FA, Kersten A, et al. Expression and functional activity of the human bitter taste receptor TAS2R38 in human placental tissues and JEG-3 cells. Molecules 2016; 21:306.
10. Wiener A, Shudler M, Levit A, et al. A database of bitter compounds. Nucleic Acids Res 2012; 40:413–419.
11. http://bitterdb.agri.huji.ac.il/dbbitter.php
12. Carey RM, Adappa ND, Palmer JN, et al. Taste receptors: Regulators of sinonasal innate immunity. Laryngoscope Investig Otolaryngol 2016; 1:88–95.

13. Huang T, Song X, Zhao K, et al. Quorum-sensing molecules N-acyl homoserine lactones inhibit trueperella pyogenes infection in mouse model. Vet Microbiol 2018; 213:89-94.

14. Bachmanov AA, Beauchamp GK. Taste receptor genes. Annu Rev Nutr 2007; 27:389–414.

15. Rennemeier C, Frambach T, Hennicke F, et al. Microbial quorum-sensing molecules induce acrosome loss and cell death in human spermatozoa. Infect Immun 2009; 77:4990–4997.

16. Deckmann K, Filipski K, Krasteva-Christ G, et al. Bitter triggers acetylcholine release from polymodal urethral chemosensory cells and bladder reflexes. Proc Natl Acad Sci 2014; 111:8287-8292.