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## Review

## Viral impacts on honey bee populations: A review

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## ABSTRACT

Honey bee is vital for pollination and ecological services, boosting crops productivity in terms of quality and quantity and production of colony products: wax, royal jelly, bee venom, honey, pollen and propolis. Honey bees are most important plant pollinators and almost one third of diet depends on bee's pollination, worth billions of dollars. Hence the role that honey bees have in environment and their economic importance in food production, their health is of dominant significance. Honey bees can be infected by various pathogens like: viruses, bacteria, fungi, or infested by parasitic mites. At least more than 20 viruses have been identified to infect honey bees worldwide, generally from Dicistroviridae as well as Iflaviridae families, like ABPV (Acute Bee Paralysis Virus), BQCV (Black Queen Cell Virus), KBV (Kashmir Bee Virus), SBV (Sacbrood Virus), CBPV (Chronic bee paralysis virus), SBPV (Slow Bee Paralysis Virus) along with IAPV (Israeli acute paralysis virus), and DWV (Deformed Wing Virus) are prominent and cause infections harmful for honey bee colonies health. This issue about honey bee viruses demonstrates remarkably how diverse this field is, and considerable work has to be done to get a comprehensive interpretation of the bee virology.

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## Contents

1. Introduction	524
2. Viral infections in honey bee colonies	524
3. Viral impacts	525
3.1. Colony level infection	525
3.2. Declines of reared honey bees	525
3.3. Impact of viruses on nutritional stress honey bees	526
3.4. Effect of viruses on foraging performance of honey bees	527
3.5. Viral effects on queen bee health	527
3.6. Effect of viruses on the honey bee's immunity	528

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4. Conclusion and future recommendation . . . . .	528
Declaration of Competing Interest . . . . .	528
Acknowledgements . . . . .	528
References . . . . .	528

## 1. Introduction

The Western honey bee (*Apis mellifera*) belongs to genus *Apis*, mainly recognized by production of honeybee products (Engel, 1999), distributed globally and well known for efficient plant pollination (Chapman et al., 2019). *A. mellifera* had been exploited by humans about 5000 years (Gisder & Genersch, 2017). The native range of *A. mellifera* comprises Africa, Europe and Middle East (Chapman et al., 2019; Tihelka et al., 2020), whereas other nine species of *Apis* are present exclusively in Asia (Han et al., 2012). Honey bees are the most important crop and wild plant pollinators (Bacandritsos et al., 2010; Cirkovic et al., 2018; Klein et al., 2006) and almost one-third (T O'Neal et al., 2018) of distinctive agricultural crops need bees pollination. *A. mellifera* is the key pollinator of several food crops (Gisder & Genersch, 2017; Tantillo et al., 2015) including vegetable, nuts, fruit as well as oilseeds (Brutscher et al., 2016; Geldmann & González-Varo, 2018). The value of these pollination services is commonly measured in billions of dollars (Goulson et al., 2015a), adding about 9.5% to the value of crops across the world (Klein et al., 2006; Potts et al., 2010a; Tantillo et al., 2015). Although wild insect pollinators as well as reared honey bees provide significant ecosystem maintenance (as pollinators of flowering plants), whereas the number of colonies (managed honey bees) has been improved globally (more than 45%) since preceding 60 years (Breeze et al., 2014; Brutscher et al., 2016; Gisder & Genersch, 2017; Goulson et al., 2015a; McMenamin & Genersch, 2015; Potts et al., 2010a). According to available published results, in the last 15 years, dramatic honey bee winter colony losses have been reported frequently from different regions all over the world (Breeze et al., 2014; Carreck & Neumann, 2010).

Pollinating insect declines portend human food safety and can affect not only apiculture (Francis et al., 2013) or agriculture but also has anthropological threats (Gisder & Genersch, 2015; McMenamin & Flenniken, 2018). It was documented that the reasons for global bees-decline are pesticides (Alburaki et al., 2018; Becher et al., 2014; Branchiccela et al., 2019; Francis et al., 2013; Goulson et al., 2015a; Klein et al., 2017; T O'Neal et al., 2018; Wells et al., 2016), destruction of habitat (Brown & Paxton, 2009; Brutscher et al., 2016; Goulson et al., 2008; Goulson et al., 2015a), industries, agriculture, parasites/pathogens (Alburaki et al., 2018; McMenamin & Flenniken, 2018), climate change (Klein et al., 2017; Sánchez-Bayo & Wyckhuys, 2019; Sihag, 2014) as well as inadequate food supply (Alburaki et al., 2018; Becher et al., 2014; Branchiccela et al., 2019; Carreck & Neumann, 2010; Chagas et al., 2019; Dolezal et al., 2019; McMenamin & Genersch, 2015; T O'Neal et al., 2018; Tantillo et al., 2015; Wells et al., 2016). Investigators demonstrated that viral infections in honey bee colonies are the main source of septicity and considered as a key risk for their health (Chagas et al., 2019; Levin et al., 2019; Remnant et al., 2017; Tantillo et al., 2015) at individual and colony level (Beaurepaire et al., 2020; Gisder & Genersch, 2015). In the 20th century, Dr. White first described honey bee viruses, while studying the filtrate of infected honey bee larvae with causative agent of Sacbrood disease (Tantillo et al., 2015). Furthermore, at least 24 viruses were known to be associated with honey bees (Chagas et al., 2019; Dolezal et al., 2016; Ellis & Munn, 2005; Gisder & Genersch, 2015, 2017; Remnant et al., 2017; Runckel et al., 2011) which remained an

important hazard to the fitness and well-being of *A. mellifera* (Dolezal et al., 2016) as well as to other honey bees worldwide (Allen & Ball, 1996; Chen & Siede, 2007; Gisder & Genersch, 2017).

Studies revealed that single strand positive (SS+) sense RNA viruses' constitute the major assemblage of honey bees infectious agents (Brutscher et al., 2015; Chen & Siede, 2007; Gisder & Genersch, 2017). Moreover, most common viruses that cause damage to bees health are: Dicistroviruses: Acute bee paralysis virus (ABPV), Kashmir bee virus (KBV), Israeli acute paralysis virus (IAPV), Black queen cell virus (BQCV) (Chagas et al., 2019); Iflaviruses such as: Deformed wing virus (DWV), Slow bee paralysis virus (SBPV), *Varroa destructor* virus (VDV1) and Sacbrood virus (SBV); and taxonomically unsystematic viruses such as: Lake Sinai viruses (LSV) and Chronic bee paralysis virus (CBPV). Last two mentioned viruses are evolutionary exclusive besides universally dispersed with LSV1-7, as well as other alternates (Brutscher et al., 2016; McMenamin & Flenniken, 2018). Similarly, *A. mellifera* rhabdovirus-1 (ARV-1) and *A. mellifera* rhabdovirus-2 (ARV-2) from the order Rhabdovirus, as well as a single double stranded DNA Filamentous virus (AmFV) were described in honey bees (Chagas et al., 2019). In this review we provided a current data and recent progress in honey bee viruses research.

## 2. Viral infections in honey bee colonies

Viruses are possibly the hidden enemies of honey bees (Ray et al., 2020) as compared to other pathogens, because most of infections pass without clinical manifestation of characteristic disease signs (Chen et al., 2006b; Martin et al., 2012). However, viral infestations had great concern (Wilfert et al., 2016), as it cause damage at various developmental stages of honey bees, like egg, larvae, pupa, adult worker, drone or queen (Chen et al., 2006a; Chen et al., 2004). In addition, clinically visible symptoms of honey bee virus diseases are mostly associated with another infectious agents, like the presence of microsporidia *Nosema apis* and strong infestations with *Varroa destructor* mites (Evans & Spivak, 2010). Viral particles spread in honey bees by two ways: by vertical and horizontal transmission (Beaurepaire et al., 2020; Chagas et al., 2019; Chen & Siede, 2007; De Miranda et al., 2012). In vertical transmission route, viruses proliferate from queen (*trans-ovarial*) or drones (*trans-spermal*) or during their mating (*venereal*) to the offspring's while in horizontal transmission route viral particles spread amongst colony members of same age generation (Chagas et al., 2019; Chen et al., 2006b; De Miranda et al., 2012) and between same and different castes (oral or by contact). According to Bowen-Walker et al. *V. destructor* mites got DWV from infested bees and behave as a carrier to spread viruses in healthy bees, when they feed upon it (vector-borne transmission) (Chen et al., 2006b; Gisder & Genersch, 2017). Researchers studied that the process of infecting or feeding on bee larvae or adult bees, these ectoparasites would appear to create an opportunity for viral particles to enter the larvae or adult bee. Under these conditions bee virus infections can be lethal (de Miranda et al., 2013). Whereas, other factors which may increase viral negative impact on bees could include environmental and nutritional stresses (Evans et al., 2009). Although, honey bee viruses typically continue as hidden contagions while showing no signs of disease but destroy bee fitness and health during favorable conditions (Tantillo et al., 2015).

### 3. Viral impacts

#### 3.1. Colony level infection

Honey bee colonies are challenged with a wide range of diseases caused by various pathogens (Alburaki et al., 2018; Chen et al., 2006b; Gisder & Genersch, 2017) and changed environmental conditions in different ways (Hao & Li, 2016). Scientists documented that areas of the world that are accountable for universal food supply had large number of colony losses annually, therefore, it is important to recognize the responsible agents. Various environmental factors having negative effect on bees fitness are: intensive agriculture with included regular pesticides use, deficiency of eminent food and loss of habitat, pathogens and pests (Brutscher et al., 2016; Goulson et al., 2015a; McMenamin & Genersch, 2015; Tantillo et al., 2015). In addition, viruses are significant threats to the honeybee colony strength (Chen & Siede, 2007; Gisder & Genersch, 2017). Colony level research points out related viruses such as ABPV, KBV, IAPV, DWV as well as LSV2 present in feeble or CCD-affected hives, however these links are not globally detected (Brutscher et al., 2016; McMenamin & Genersch, 2015). CCD (Colony collapse disorder) is categorized with quick extinction of adult bees from hive and finally queen remains with few newly emerged bees (Evans et al., 2009; McMenamin & Genersch, 2015) while consequent damage was valued about 75 billion dollars, both to agriculture as well as apiculture, globally (Tantillo et al., 2015). Studies revealed that IAPV was related to CCD (Tantillo et al., 2015) because its presence in a honey bee colony is linked with high threat to colony collapse (Genersch & Aubert, 2010; Meixner, 2010). Similarly, KBV was also detected in colonies showing CCD signs (Brutscher et al., 2016; de Miranda et al., 2010; McMenamin & Flenniken, 2018; Tantillo et al., 2015).

The severe infection of KBV and ABPV results in the excessive loss of adult bees. Consequently, it results in the emergence of infected pupae and larvae and lack of adults to look after the young brood. ABPV aggregates in the hypopharyngeal glands (Chagas et al., 2019) and brain, while KBV and ABPV were determined in fecal material and were transmitted through various routes, such as oral communication (larvae, adults, cannibalism, fecal material or contaminated diet) (de Miranda et al., 2010). Furthermore, transmission through live vectors as *V. destructor* or *Tropilaelaps* spp. mites results in the remarkable spread of viruses (De Miranda et al., 2012), e.g. DWV in an individual bee (Tehel et al., 2016) as well as in the whole colony (Amiri et al., 2015; de Miranda et al., 2010; Genersch et al., 2010; Goulson et al., 2015a; McMenamin & Flenniken, 2018). Due to high spread rates, DWV is more extremely described virus in *A. mellifera* (Goulson et al., 2015a; Schittny et al., 2020) if compared to other bee species (Tehel et al., 2016). Similarly, DWV-A (deformed wing virus type A) and DWV-B (deformed wing virus type B) were responsible for winter colony losses (Highfield et al., 2009).

According to published results, KBV and IAPV were initially linked with CCD but further research revealed that not a single virus was responsible for it (Barron, 2015; Cornman et al., 2012; McMenamin & Flenniken, 2018). In the same way, data collected in Spain, Belgium and US (both affected and non-affected CCD colonies) have shown numerous LSVs which are spread worldwide and occasionally responsible for infections of honey bee colonies (McMenamin & Flenniken, 2018; Remnant et al., 2017). Likewise, long time disclosure to various stresses causes fall of wild bee pollinators populations number and colony destruction. But the effect of these factors is different and depends on geographical area (Goulson et al., 2015b). Research has exposed that SBPV was correlated with colony collapse in England, but mostly less prevalent in other European apiaries (Carreck et al., 2010; De Miranda et al.,

2012). SBPV not only primarily affects the fore legs (paralyses) of honey bees but also found in head, salivary gland, mandibular and hypopharyngeal glands, crop, fat body, while present in thorax, midgut, hindlegs and rectum in low quantity (De Miranda et al., 2012). ABPV and DWV were present in honey bee colonies before the appearance of parasitic mites in UK and were responsible for colony destruction but rarely (Sánchez-Bayo et al., 2016). Furthermore, *V. destructor* mites as well as viral pathogens were both responsible for colony failure (Francis et al., 2013; Genersch, 2010), as without mites, viruses were unable to cause honey bee colony collapse (Sánchez-Bayo et al., 2016).

Moreover, research also has revealed that CCD in USA was caused by IAPV (De Miranda et al., 2012; Genersch, 2010; Hou & Chejanovsky, 2014) while it was not mentioned in Australia which is free of *V. destructor* mites. Likewise, KBV also enhance in the presence of strong infestations of *V. destructor* mites but causes losses in beekeeping also in Australia (Sammataro et al., 2000). Moreover, *V. destructor* together with DWV were deliberated as evolving infection and showed dangerous results (Chagas et al., 2019; McMenamin & Genersch, 2015; Tantillo et al., 2015) both in individual bees and colonies (Chen & Siede, 2007; Dalmon et al., 2019; Francis et al., 2013; Genersch & Aubert, 2010; Gisder & Genersch, 2017). An inquiry from Thailand showed that in varroa mites' samples, DWV were present in 100%. In the same way, parasitic mites collected from honey bee colonies in France were 100% and in Poland 69% positive for DWV (Tantillo et al., 2015). According to GBMP (German bee monitoring project) the existence of DWV in hives had the better indication of colony impermanence as compared to KBV and ABPV (Francis et al., 2013). CBPV is highly distributed in England (Chen & Siede, 2007) and reports from Austria acknowledged that because CBPV were present in diverse geographic area and virus was determined in 10% of different disease-ridden colonies (Berényi et al., 2006; Chen & Siede, 2007). Another study from Thailand suggested that *V. destructor* was accountable for various viral infections (DWV, ABPV, BQCV, KBV and SBV) in beehives (Chantawannakul et al., 2006).

It was demonstrated that BQCV had been highly spread and responsible for colony losses of *Apis cerana* in Thailand, South Korea, Japan, China and Vietnam (Chantawannakul et al., 2016; Yang et al., 2013) as well as of *A. mellifera* in Vietnam, South Korea, Thailand, China, Japan (Ai et al., 2012) and also caused infection in *Apis dorsata* and *Apis floreae* populations in Thailand and China (Chantawannakul et al., 2016; Mookhploy et al., 2015; Zhang et al., 2012). Additionally, parasitic mite associated viruses such as DVW, IAPV (Francis et al., 2013) and ABPV caused colony mortality (Chen et al., 2006a; Hou & Chejanovsky, 2014; Martin, 2001; Tentcheva et al., 2004) and their virulence might be enhanced when *V. destructor* acted as vector for their transmission (Molineri et al., 2017). After infection, these viruses cause shaking, restrain the movement of bees and loss of workers within two days (Amiri et al., 2017). Furthermore, IAPV was reported in every developmental stage of honey bee and its infection was observed almost in all tissues, but mostly existed in hypopharyngeal glands, alimentary canal and nervous system (Amiri et al., 2019; Chen et al., 2014; De Miranda et al., 2012). It was documented that *V. destructor* feeds upon bee brood as well as adults and behaves as a carrier for various honey bee viruses (Chagas et al., 2019; Tantillo et al., 2015).

#### 3.2. Declines of reared honey bees

Managed honey bees are in decline because of numerous interacting agents including parasite and pathogen pressure (Carr-Markell et al., 2020; Hellerstein et al., 2017), pesticide exposure (Carr-Markell et al., 2020; Ferrier et al., 2018; McMenamin &

Genersch, 2015; Ratnieks & Carreck, 2010; Tantillo et al., 2015; Wells et al., 2016; Williams et al., 2010) and territory demolition as well (Chagas et al., 2019; Goulson et al., 2015a; Potts et al., 2010a; Smith et al., 2015). It has been reported that viruses of honey bee can be transmitted to another bee species (Gisder & Genersch, 2017) and are responsible to their declines (Graystock et al., 2015). Studies have shown that population of European reared honey bees are in decreasing trend (Potts et al., 2010b) while there is regular fall of colony number in middle European states (Amiri et al., 2015; Antúñez et al., 2017; Van der Zee et al., 2012) whereas slightly increase in Mediterranean countries (Ball, 1996; Goulson et al., 2015b). BQCV was common in managed honey bee population in North America (Desai et al., 2016) and Europe (McMahon et al., 2016). A study of 26 sites from England revealed that, BQCV was more prevalent in the honey bees as compared to bumble bee species (McMahon et al., 2015). Similarly, IAPV was widespread in honey bees in North America, while it was occasionally noticed in European apiaries (Cox-Foster et al., 2007; Tehel et al., 2016). Research stated that viruses can be transmitted among wild bees and managed bees and opposite (Brutscher et al., 2016; Galbraith et al., 2018; Graystock et al., 2016; McMenamin & Flenniken, 2018; Murray et al., 2019). Furthermore, viral particles can be multiplied within and spread among different bee species and their infection level depends on either viral strain or host (Tehel et al., 2016) as well as some other features, including host sex, nutritive status, genetic makeup and age (McMenamin & Flenniken, 2018).

The consequence of viral infection in wild bees include body malformation (Genersch et al., 2006), diminish reproductive capability, efficient septicity and susceptibility to death (McMenamin & Flenniken, 2018). It has been reported that transmission of IAPV from reared honey bees to wild bees can be the consequence of common usage of flowers during foraging (Tehel et al., 2016). IAPV was noticed to be spread from *A. mellifera* to *A. cerana* (Theisen-Jones & Bienefeld, 2016). Conversely, ABPV most commonly present in wild bees as compared to managed honey bees, was possibly transmitted from wild bees to the *A. mellifera* (Tehel et al., 2016). Additionally, Chinese SBV had triggered severe damage in *A. cerana* managed colonies in Asia (Steinhauer et al., 2018). ABPV was prevalent commonly in South America and Europe, while IAPV in Australia and Middle East alongside KBV in North America and New Zealand. Besides, the titers and frequency of KBV and ABPV enhances in late summer while ABPV particles increased their titer earlier than KBV, depend upon the colony progression level (de Miranda et al., 2010). Main symptoms of honey bees CBPV Type I disease are trembling wings and bodies, ataxia, circling, inability for fly, crawling on ground and up grass streams and mortality; and CBPV Type II syndrome include blackening and withdrawal of hair from the thorax and abdomen, small-shiny-dark bees and finally loss of highly paralyzed adults (de Miranda et al., 2010; Tantillo et al., 2015). In south American countries like Uruguay, Brazil and Chile, many viruses of honey bee had been detected in apiaries, also exist in moderate environment (Molineri et al., 2017). Study from Denmark revealed that, winter colony losses exceeds near 32% from 2007 to 2008, that were mostly correlated with *V. destructor* infestations and viral particles association (Amiri et al., 2015; Nielsen et al., 2008; Vejsnæs et al., 2010).

Moreover, about 14% colony losses were reported in Greece in 2007 to 2008 (Bacandritsos et al., 2010). Similarly, Thailand Sacbrood virus (TSBV) was responsible for the loss of 90% of managed *A. cerana* bees in India (Theisen-Jones & Bienefeld, 2016), Kashmir, Japan, South Korea, Thailand, Nepal, Vietnam, China (Forsgren et al., 2015) and also observed to cause infestation in *A. florum* and *A. dorsata* in India (Allen & Ball, 1996). In addition, DWV was more widespread than SBV in *A. mellifera* population, reported from Thailand, Sri Lanka, Japan, Nepal, Vietnam, and China (Ai

et al., 2012; Forsgren et al., 2015). While Uganda and Turkey were considered to be SBV free and no particle of SBV was reported in honey bee population (Beaurepaire et al., 2020). Besides, DWV infestation in *A. cerana* has been determined in Japan, China, Vietnam, and South Korea (Forsgren et al., 2015) in *A. dorsata*, and *A. florum* population in China (Chantawannakul et al., 2016; Zhang et al., 2012). DWV was isolated from *A. dorsata*, *A. florum* and *A. mellifera* revealed that it is transmitted from *A. mellifera* to *A. dorsata* and *A. florum* in China through common pollinating resources (Forsgren et al., 2015). Moreover, Serbian apiaries showed high level of DWV incidence as compared to further countries like Slovenia, Hungary, Austria, Uruguay and France (Cirkovic et al., 2018). In Croatia before affiliation to European Union most of honeybee viruses were detected in lower levels than in its neighboring countries (Gajger et al., 2014; Tlak Gajger et al., 2014). In last few decades many different diagnostic methods were developed or improved (Schurr et al., 2017). Also, two plant infecting viruses such as Turnip ring spot virus (TuRSV) and Tobacco ring spot virus (TRSV) were also detected in honey bees (Granberg et al., 2013; Li et al., 2014; McMenamin & Genersch, 2015).

### 3.3. Impact of viruses on nutritional stress honey bees

The impact of quality and amount of food in mammals mark their exposure to environmental stressors and pathogens (Dolezal & Toth, 2018). In the same way, this fact in honey bees is not well known (Goulson et al., 2015a). However, nectar and pollen contain different ingredients: carbohydrates, proteins and lipids, other phytonutrients and essential substances (vitamins and minerals) having optimistic influence on their immune system (Di Pasquale et al., 2013; Goulson et al., 2015a). Additionally, various food resources hold important effect on bees health (Dolezal & Toth, 2018). Furthermore, nectar and pollen are necessary for larvae and adult bees providing vital nutrient's for survival. Whereas, poor nutrition results in less bee foraging capability and has negative impact on individual and colony level (Leach & Drummond, 2018; Steinhauer et al., 2018). Studies have shown that, variety of pollen has great effect to standardize of the inborn immune system and decreases mortality rate which are the consequences of visible IAPV infections (Dolezal & Toth, 2018) and *N. ceranae* attack (Leach & Drummond, 2018). Other nutrients like proteins, vitamins and minerals play an important role and enhance bee's life span (Dolezal & Toth, 2018). The access of bees to food resources is now alarming because alteration of land practice marks the change of floral properties, retain negative impact on bee physiology and health. Moreover, hives bounded by more cultivated land result high colony losses (Dolezal et al., 2019; Steinhauer et al., 2018) and decrease fat assemblage arriving winter time (Dolezal & Toth, 2018).

Though, this fact is not always true because in some cases higher crops growing consequently decrease pollen storage as well as production of honey (Sande et al., 2009). Whereas, a study from western United State of America revealed higher honey production in cultivated areas as compared to urban regions (Brodschneider & Crailsheim, 2010; Dolezal & Toth, 2018). *N. apis* and *N. ceranae* infections of honey bees cause the disturbance in digestion and also effect immunity of the host, which consequently lead to bees malnutrition as well as immunosuppression and susceptibility to additional viral pathogens infections, like SBV (Dolezal & Toth, 2018) and large number of DWV particles (Dolezal et al., 2019). The infection of pathogens (e.g. SBV and *Nosema* spp.) cause decline of nutritional value in a honey bee colony like lower collection of pollen and less storage of vitellogenin, and enhance immature bee's hormone level (causes premature foraging behavior) (Dolezal & Toth, 2018; Goblirsch et al., 2013). Various environmental factors such as imbalance nutrition and pathogens infection

cause honey bee colony disorganization, depopulation and mortality (Dolezal & Toth, 2018).

Additionally, the reduction of protein level in honey bees, weakens their immune system and vulnerable to viral attack (Evans & Schwarz, 2011). In another study, it was reported that like Nosemosis, viruses also associated with digestive system of bee's, interrupt digestion, physiology and nutritional requirements of host (Dolezal & Toth, 2018). As digestive system acts as a reservoir for viral titers because most activities occur there like pollen storing, nectar dispensation and other metabolic activities (De Miranda et al., 2012). Moreover, lower quality of food intake consequently higher DWV titer in bees as compare to higher quality of pollen holding food (DeGrandi-Hoffman et al., 2010). Though, the correlation between food quality and DWV contamination need additional research, as other studies revealed that, DWV titer were found more in pollen containing diet consuming by bees as compare to nutrients comprising sucrose foodstuff (Alaux et al., 2011; Grozinger & Flenniken, 2019). Due to lack of pollen supply, bees cannibalize their young brood to get proteins (De Miranda et al., 2012) while feed on old larvae upon them (Brodschneider & Crailsheim, 2010) that lead to the possible cause of oral exchange of viral particles (De Miranda et al., 2012).

### 3.4. Effect of viruses on foraging performance of honey bees

Honey bees are the major managed insect pollinator worldwide (Abou-Shaara, 2014; Calderone, 2012; Gisder & Genersch, 2017; Joseph et al., 2020) while wild bees can also improve yields of various crops and are a key part of natural ecosystems (Aizen et al., 2009; Garibaldi et al., 2013). Honey bee (*A. mellifera*) is an important player in farming and pollinate a large number of food crops (Ferrier et al., 2018), which add more than 15 billion dollars to the market per year (Chen et al., 2006a,b; Morse & Calderone, 2000). Nowadays since there is gradual decline in bee populations over the world, there is great emphasis on bee survival because bees are beneficial and famous for their pollination services, to supply foodstuff (e.g. fruits, nuts, berries, seeds, leaves and roots) (Hung et al., 2018). Besides human, they also pollinate foods eaten by other animals and birds worldwide (Chagas et al., 2019; Hung et al., 2018). Varroa mites feed upon honey bees and introduces high concentrations of viruses to their host, and causes different alterations such as body weight loss, suppressed immunity, short life span and diminishes foraging capacity (Amiri et al., 2017). Additionally, DWV attack on those areas of brain, that controls sense of smell and had negative influence in the foraging behavior of honey bees (Klein et al., 2017). DWV infected bees without physical deformities, fly to a short distance and flight duration as compared to non-infected bees. DWV decrease the gene countenance which control memory as well as wing development together with olfactory learning (Wells et al., 2016).

Viruses from Dicistroviridae family and CBPV create severe manifestations in adult bees and decline the life span of workers if viral titers increased up to maximum level (de Miranda et al., 2010; Ribière et al., 2010). Whereas, SBV and DWV as well as BQCV are present and persist in honey bees with no outward affliction signs. But turn out to be troublesome when they get suitable conditions (biotic or abiotic) for replication (Amiri et al., 2015; Chen & Siede, 2007; Dainat et al., 2012; Prisco et al., 2011). In addition, CBPV aggregate, multiplies, damage and disturb the brain area (CNS) of honey and their neuronal function responsible for sensory perception (Ribière et al., 2010). As result the infected honey bee vibrating, crawling at the hive entrance and is unable to fly (De Miranda et al., 2012). Scientists discovered a new virus called Kakugo virus (KV) which was isolated in Japan from the brain of worker bees in 2004 (Fujiyuki et al., 2004) that had similarities with DWV (about 98% at the nucleotide level) (Terio et al., 2008).

In addition, the brain tropism was noticed (specifically in antennas, in optic neuropils and in mushroom bodies) (Shah et al., 2009), which controlled sense experiences and organized the performance in bees (De Miranda & Genersch, 2010; Tantillo et al., 2015).

### 3.5. Viral effects on queen bee health

Pathogenic viruses are extremely hazardous to honey bee health and can cause colony losses (Martin et al., 2012; Mondet et al., 2014; Remnant et al., 2017). Besides, disease causative agents, the death of queen has been considered as one of the major factors for colony failure. Because presence of queen for a colony is crucial, not only to lay eggs but to coordinate colony members tasks and behavior through pheromone secretion (Brutscher et al., 2019). Likewise, other colony members, the queen bee also acquires and faces the attack of pathogenic viruses (Amiri et al., 2017) and contain many viruses (up to six) at a time (Beaurepaire et al., 2020). It was documented that drones were able to transmit DWV to queen when infected drones come to the mating area and introduced contaminated semen to queens (Amiri et al., 2017; Brutscher et al., 2019; Chen et al., 2006b). Additionally, the presence of viral titers in the reproductive system of drone and queen (Chen et al., 2006a; Chen et al., 2006b) and semen, demonstrate viral transference through sexual intercourse in bees (De Miranda et al., 2012; Tantillo et al., 2015). Infected queen can transfer viral particles directly (vertically) to her brood (Amiri et al., 2017; Schittny et al., 2020; Tantillo et al., 2015). Vertical conveyance of viruses occur through already infected ovarian tissue of queen bee or by fertilization of egg by infected sperms (De Miranda et al., 2012; Tantillo et al., 2015). Study directed by Chen and collaborators revealed the existence of BQCV and DWV in the digestive tract of queen bee (Amiri et al., 2017; Tantillo et al., 2015). DWV can infect young and adult queens, but is less prevalent in young ones (Delaney et al., 2011). It infects queens gut, head, ovaries, fat body (Amiri et al., 2016) and can cause clinical visible characteristic disease sign in form of deformed wings (Amiri et al., 2017). As a result, due to high contamination of viruses in queen ovaries, causes ovary degeneration and may the source for deposited sperm mortality (Gauthier et al., 2011).

Consequently, failure in reproductive capability might be effect hive accomplishment, efficiency and replacement of queen (Amiri et al., 2017). Furthermore, SBV was also observed in the embowelled body and ovary of queen bee but its transmission and negative impact was not well understood (Amiri et al., 2017; Ravoet et al., 2015). BQCV can be responsible for the decease of honey bee queen larvae, and cause infection in queen pupa (Tantillo et al., 2015). BQCV particles were detected in the ovary, and gut of queen bee (Amiri et al., 2017). Additionally, like other viruses BQCV was also detected in *A. mellifera* globally (Allen & Ball, 1996; Ellis & Munn, 2005), where it caused covert infestation in brood and adult worker bees (De Miranda et al., 2012). The presence of DWV and BQCV in queen bee digestive tract showed that viral titer must ingested by queen through contaminated food (Tantillo et al., 2015), that was the suitable environment for viral proliferation and can be easily transmitted to other tissues (spermatheca, ovaries, hemolymph) by penetrating wall of the tract (Chen et al., 2006b). Recent finding have shown that IAPV was transmitted from infected workers to queen bee through prophylaxes and direct contact with infected bees (Amiri et al., 2019).

BQCV is currently the most important and widespread virus in *A. mellifera* (Chagas et al., 2019; Gauthier et al., 2007) globally. Additionally, BQCV was reported in Japan, China and Thailand in local honey bee populations of *A. c. japonica*, *A. c. indica*, *A. florea* and *A. dorsata* (Gisder & Genersch, 2017). Furthermore, BQCV has partial stress on worker as well as on drone bees (Amiri et al., 2015; Retschnig et al., 2014). Experimental evidences confirmed

the simultaneous presence of DWV and BQCV in queen bee, and were also detected in her eggs, larva's as well as adult workers and suggested that, it can be transferred vertically (Chen et al., 2006b; Tantillo et al., 2015). Similarly, ABPV particles in outwardly normal drone bee's semen indicated that, the virus can be transmitted from drone to queen bee through mating. Furthermore, CBPV was also determined in queen bee as well as in its developing stages and it was assumed that CBPV can be transmitted vertically (Tantillo et al., 2015). These results showed that most viruses were problematic for queen health but some revealed no visible signs of infection and they were easily spread by queen to their offspring. Generally, viruses had less effect on queen health but these prognosis require further research to investigate their association with colony fitness and queen health (Amiri et al., 2017).

### 3.6. Effect of viruses on the honey bee's immunity

The transmission of viral particles from parasitic mites to honey bees suppresses the immunity of bees or increase the virus virulence and infectiveness. Additionally, the *V. destructor* saliva contain immunosuppressive proteins and intimidate the immune system of infested honey bees (Meixner, 2010; Tantillo et al., 2015). The parasitic mites infestation on honey bee, destroy its body's mechanical defenses and it becomes exposed to further viral attack (Tantillo et al., 2015). The strong virus infection encourages virulence increase in honey bees, suppress their immunity, and consequently make them vulnerable after exposures for other environmental stresses (Sánchez-Bayo et al., 2016). Similarly, organosilicon spray complementary (used in several pesticide preparations) destroy honey bees olfactory learning and enhance viral multiplication (T O'Neal et al., 2018). The neonicotinoids also disrupt the immune and reproductive system functions of honey bees (Gajger et al., 2017; Piironen & Goulson, 2016), consequently enhances multiplication of DWV in bees (Di Prisco et al., 2013; Goulson et al., 2015a). It was also reported that high amount of DWV titers in honey bees inhibits their immune responses and melanin production, leading to propagate *V. destructor* mites and enhances its progeny as well (Gisder & Genersch, 2017). Furthermore, *V. destructor* septicity subsidize to the suppression of bee host immunity, and enhances the infections with DWV (Genersch, 2010; Gisder & Genersch, 2017; López-Urbe & Simone-Finstrom, 2019) and ABPV (Molineri et al., 2017).

## 4. Conclusion and future recommendation

Beekeeping is more dependent on complex environmental factors than any other animal or food production industry. Although knowledge of honey bee viruses is still limited compared to other well-studied insect viruses, such as Baculo viruses, hence understanding of virus infections in honey bees are of great concern. In last few decades a global uncontrolled inter- and intranational exchanges and trade of honey bees and other goods have led to the spread of viral diseases to new geographical areas. Much work has been done regarding honey bee viruses' identification, spread, history, physiochemical characteristics and infections etc. Observation of pollinators is instantly crucial to notify managing approaches and both beginning as well as advanced beekeepers should learn to recognize and control honey bee diseases. By implementing of One health approach through good veterinary, beekeeping and environmental practices can be guarantee for safety of beehive products, as well as, sustainable apiculture and insects pollinators health protection patterns. Scientists and researchers from all over the world, recommend special suggestions for consistent policies that should be implemented globally to support beekeeping and its management in future.

## Declaration of Competing Interest

The authors declare that they have no known competing interests.

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