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BIOMEDICINES-CINA AGAINST COVID-19: CONTROLLED PLANT DISEASES ENRICHED SCIENCE AND TECHNOLOGY COMMUNICATION GREEN ECONOMY



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ABSTRACT

The economic-plant-mulberry is infected by different pathogens causing diseases and significantly reduces silk production. Though pesticides are the most effective means of control, but they are expensive and not environment friendly. On the other hand, the ongoing spread of the novel coronavirus, forming epidemic, affecting human civilizations, because recently, no appropriate antiviral drugs for effective treatments or vaccines against COVID-19. To meet the challenge, it is reported that the therapeutic value of traditional-, complementary- and alternative-biomedicines-Artemisia nilagirica, has been used for centuries, to overcome various medical disorders. So, to concur with the situation, it will require new and more efficient solutions, technologies, and products. Present pretreatment with ultra-high-diluted biomedicines-Cina, prepared from the flowering meristems of Artemisia nilagirica (Clarke) pamp, mixed with water at an extremely low dose, were applied by foliar spray once daily for 15 days @ 10 ml/plant, against naturally occurring, root-knot-, leaf spot-, powdery mildew-, mosaic- and tukra- mulberry diseases, in field trials and silkworms rearing. Pretreatment-investigations have revealed that ultra-high-diluted-Cina, highly effective in ameliorating different mulberry-diseases by inducing their natural defense-response against pathogens-infection and leaving no residual-toxicity in the leaves to affect the growth of silkworms also. It can be concluded that the ultrahigh-diluted, eco-friendly easily-available, easily applicable-Cina, at an extremely low dose, not only used as a potential-biomedical-drug against various plantdiseases, by inducing natural-defense- response, but also, it may be effective against COVID-19 for vaccinations and clinical trials by boosting the natural immune system for the improvement of Science and Technology communication cost-effectiveness green-economy and biodiversity conservations as well as bioapplications issues. And the future clinical-scientists develop all aspects of clinicalcase-reports by publishing in the appropriate medical research archives, with the sincere hope that this crisis will soon be over and the whole world, may fight against the COVID-19 war, retaining normal forms of human civilizations globally.

1. INTRODUCTION

The mulberry, is a major foreign exchange earner of India, which is short about 30% to fulfill the home requirements [1], due to the mulberry diseases, caused by pathogens, which affects the silk -yield in terms of quality and quantity [1], [2], [3], [4], [5], [6], [7], [8], [9], [10], [11], [12], [13], [14], [15], [16], [17], [18], [19], [20], [21], [22], [23], [24], [25], [26], [27]. Synthetic and chemical pesticides are the most effective means of control, but they are © 2020 The Author(s). This is an open access article distributed under the terms of the <u>Creative Commons Attribution License</u>, which permits unrestricted use, distribution, and reproduction in any medium, provided the original author and source are credited.

both expensive and environmentally unfriendly, toxic to man and not-biodegradable [28], [29]. The use of plant extracts affects our biodiversity conservation [30], [31], [32], [33], [34] and climate change will determine future food security [35]. Cropping pattern [35], [36], and expert comments are applied to achieve sustainable agriculture in the future [35], [36]. Currently novel coronavirus disease- COVID-2019 epidemic problems, identified by the Chinese authorities [37], forming pandemic with profound effects on our private and professional life, the world economy, and the social life and humanity [38] with unusual viral pneumonia [39] and scientists are working with the genome of COVID [40], [41] which could potentially emerge in humans in the future [41]. For this, WHO, responses to the outbreak[37] and warns, for this virus is going to stay among humans for a long time, [41] which has currently no effective treatment [42], [43] due to genetic resistance [44], sufficiently divergent for the future evolution, adaptation, and spread of virus [45]. So, current views on economic impact on India, beyond, and global is going to be steep [46], [47] and it is likely to offers a cure or at least a vaccine [46], [47] due to the pandemic situation is analogous to war and the delay of every week in the deployment of a vaccine to the seven billion humans on earth will cost thousands of lives [48]. Antimalarial drugs widely used against COVID-19 heighten the risk of cardiac arrest. How can doctors minimize the danger? [49].

A number of plant bioagents- or – nematicides [2], [35], [36], intercropping-[50] and crop rotation-, animal bionematicides [34], [51], [52], [53], and biomedicines, only stand as a suitable- and useful- against different plants-, animals- and human- diseases caused by pathogens[2],[4], [8], [10], [17], [20], [21], [24], [51], [52]. But it remains a problem of biodiversity conservation green economy applications and not always cost-effective [34], [51], [53]. Now, the traditional medicine [54], [55], [56], [57], [58] 'Indian wormwood'- *Artemisia nilagirica*, is considered for centuries against diseases. The clinical biomedicines; Cina, is being used traditionally to overcome more than 50medical complications due to its low toxicity and high efficacy [11], [14], [15], [22], [25], [33], [54], [59] and it is highly effective in ameliorating different plan and animal diseases [5], [7], [11], [12], [14], [15], [22], [25], [59].

The aims and objectives were to investigate new and more efficient solutions, technologies and products for controlling disease, by using an ultra-high diluted biomedicines-Cina with pretreatment, against naturally occurring, root-knot-, leaf spot-, powdery mildew-, mosaic- and tukra- diseases of mulberry, in field trials and silkworms rearing, which influence for the development ideas of vaccines and treatments against coronavirus disease (COVID-19) outbreak by using these ultra-high diluted biomedicines-Cina at an extremely low dose, which may resist the COVID-19 by boosting our immune system.

2. MATERIALS AND METHODS

2.1. PREPARATION OF BIOMEDICINES-CINA MOTHER TINCTURE (MT)

Air-dried and powdered flowering meristems of *A. nilagirica*, (Plate 1), were extracted with 90% ethanol and the crude residues were dissolved in 90% ethanol at 1mg/ml concentration and were formed homeopathic mother tincture of *A. nilagirica* called Cina MT (Original Solution or Crude Extract i.e. Mother Tincture) [5], [7], [11], [16], [18], [22], [25], [33], [60].

2.2. PREPARATION OF HIGH DILUTED LIQUID BIOMEDICINES-CINA 30C AND -CINA 200C MEDICINE

The crude extract of *A. nilagirica*, named Cina MT were diluted with 90% ethanol (1:100) proportionate in a round vial which was filled up to two-thirds of its space, tightly corked and then were given 10 powerful downward strokes of the arm, forming the 1st centesimal potency named Cina1C and all the subsequent potencies were prepared in this way; -Cina 30C and -Cina 200C medicine were prepared respectively [5], [7], [11], [16], [18], [22], [25], [33], [60].

2.3. PREPARATION OF MEDICATED BIOMEDICINES-CINA 30C AND -CINA 200C GLOBULES

By the few drops of a liquid potency of; -Cina 30C and -Cina 200C, were prepared respectively [5], [7], [11], [16], [18], [22], [25], [33], [60].

2.4. PREPARATION OF MEDICATED CONTROL GLOBULES

Cina 30C and -Cina 200C, [5], [7], [11], [16], [18], [22], [25], [33], [60] by the same way.

2.5. PREPARATION OF ULTRA HIGH DILUTED BIOMEDICINES-CINA30C AND-CINA 200C PRETREATMENT TEST- AND CONTROL- SOLUTIONS

By mixing with sterile distilled water in the proportion of 7.2 mg globules/ml of water respectively [5], [7], [11], [16], [18], [22], [25], [33], [60].

2.6. MORTALITY TEST

For the assessment of the direct effect of; -Cina 30C and -Cina 200C pretreatment - test solution [5], [7], [11], [16], [18], [22], [25], [33], [60].

2.7. SITE OF THE PRETREATMENT EXPERIMENTAL PLOTS

The field experiment was carried out at the Sriniketan Sericultural Composite Unit, India where throughout the year, the whole mulberry field was naturally infected with root-knot disease of mulberry plants (*Morus alba* L., cv. S1) caused by *Meloidogyne incognita* (Kofoid & White) Chitwood, root-knot nematodes pathogens and every year in September-October occurrence of four foliar diseases were seen and these were: leaf spot disease caused by *Cercosporam moricola* (Cooke) fungus pathogens, powdery mildew disease caused by *Phyllactinia corylea* (Pers.) Karst fungus pathogens, mosaic disease caused by mosaic virus pathogens, and tukra disease caused by *Maconellicoccus hirsutus* (Green) mealybug pathogens [2], [4], [7], [8], [10], [18], [20], [22], [24], [27].

2.8. ESTIMATION OF THE NEMATODE PATHOGEN POPULATION

Soil and root samples [28], [29], [31], [59], [60], [61], [62] were taken at random to determine the extent and intensity of *M. incognita* -pathogen infestation [2], [4], [7], [8], [10], [18], [20], [22], [24], [27].

2.9. PREPARATION OF FIELDS

The first soil, was mixed with the yard manure (2:1 vol/vol), and were assessed the *M. incognita population* [2], [4], [7], [8], [10], [18], [20], [22], [24], [27] and this naturally infected soil-filled area, demarking the pretreated field, replicated thrice [2], [3], [6], [7], [8], [9], [10], [11], [12], [13], [14], [15], [16], [17], [18], [20], [25], [53].

2.10. PLANTATION OF MULBERRY CUTTING

Mature three years old mulberry cutting, *Morus alba* L., cv. S, were planted and allowed to grow for a period of three months [2], [3], [4], [7], [8], [10], [11], [12], [13], [14], [15], [16], [17], [18], [20], [21], [22], [24], [25], [26], [27].

2.11. DIVISION OF GROUPS AND PLOTS

After three months of growth of mulberry, the *M. incognita* population was estimated in the soil as well as roots [28], [29], [31], [59], [60] and the plants were allowed to grow for a period of 137, replicated three times [2], [3], [6], [7], [8], [9], [10], [11], [12], [13], [14], [15], [16], [17], [18], [20], [25], [53].

2.12. PRETREATMENT WITH HIGH DILUTED BIOMEDICINES-CINA30C AND -CINA200C -TEST AND - CONTROL SOLUTIONS

Seventy-six days after pruning, of mulberry plants, all the pretreatment was done by foliar spray @10 ml/plant (7.2 mg/ml concentration) once daily for 15 days with -Cina 30C and -Cina 200C -test solutions and -control solution respectively [5], [7], [11], [12], [13], [14], [15], [16], [18], [22], [25], [33], [60]. At fifteen days after the last pretreatment, all the parameters of diseases were assessed again for each group [5], [7], [11], [12], [13], [14], [15], [16], [18], [22], [25], [33], [60] and all the data were used for statistical analysis by Student's t-test [2], [3], [6], [7], [8], [9], [10], [11], [12], [13], [14], [15], [16], [17], [18], [20], [21], [22], [23], [24], [25], [53].

2.13. ANALYSIS OF RESIDUE

The residues run in a thin layer chromatography plate (TLC) with the standard; - Cina 30C and Cina 200C, - pretreatment test substances respectively [5], [7], [11], [12], [13], [14], [15], [16], [18], [22], [25], [33], [60].

2.14. PLANT PATHOGENS CAUSED MULBERRY DISEASES

Root-knot Disease were assessed by the; total number and surface area of leaves and root-galls / plant [2], [3], [6], [7], [8], [9], [10], [11], [12], [13], [14], [15], [16], [17], [18], [20], [21], [22], [23], [24], [25], [53]. The total protein content of the leaf and root were determined [31], [32]. All the data from experiments were counted for statistical analysis by the student's t-test [2], [3], [6], [7], [8], [9], [10], [11], [12], [13], [14], [15], [16], [17], [18], [20], [21], [22], [23], [24], [25], [53]. Every year in September-October occurring, the different foliar diseases, observed in the sericulture field, were: leaf spot disease, tukra disease (Plate 3), powdery mildew disease (Plate 4) and mosaic disease (Plate 5). All the diseases identified according to their characteristic symptoms by the experts concerned [26], [27], [30].

2.15. REARING OF SILKWORMS

The eggs of a mother moth of the multivoltine 'Nistari' race (*Bombyx mori* L.), after hatching and brushing 1st stage silkworm larvae in the rearing tray [1],[2], [3], [4], [7], [8], [9], [10], [11], [12], [13], [14], [15], [16], [17], [18], [20], [21], [22], [23], [24], [26], [27], [63], [64], [65]. Mulberry leaves were used for feeding fifteen days after the last pretreatment with biomedicines; Cina 30C and Cina 200C, respectively. The fresh silk gland weight of mature 5th instars larvae (Plate 6) (before start spinning), starting time to spinning (Plate 7), span of spinning, fresh cocoon weight, fresh shell weight, silk layer ratio (SR % = Shell weight / Cocoon weight X 100), effective rate of rearing (ERR % = Number of cocoon harvested / Number of silkworms hatched X 100), sex ratio percentage (Number of male adults emerged X 100) and egg-laying capacity of mother moth were determined [1],[2], [3], [4], [7], [8], [9], [10], [11], [12], [13], [14], [15], [16], [17], [18], [20], [21], [22], [23], [24], [26], [27], [63], [64], [65]. All the data from the rearing trial were used for statistical analysis by the student's t-test.

2.16. SCIENCE AND TECHNOLOGY COMMUNICATION GREEN-ECONOMY APPLICATIONS

The activity and the importance of "Pretreatment with Ultra High Diluted biomedicines; Cina 30C and Cina 200C, at an Extremely Low Doses, Use as Potential Cost-Effective Biomedicines Against Various Pathogens including COVID-19: Enriching Science and Technology Communication Green-economy Applications and Healthcare-, Defense response- and Immunity- as well as Biodiversity Conservation- Issues" in different audiovisual media (TV channels), social media, web pages, newspapers, and journals are recorded, which is a platform to promote and discuss different new issues and developments by publishing [1],[2], [3], [4], [7], [8], [9], [10], [11], [12], [13], [14], [15], [16], [17], [18], [20], [21], [22], [23], [24], [26], [27], [63], [64], [65], [66], [67].

2.17. FUTURE IDEAS OR SUGGESTIONS IN RESEARCH

It will be achieved from typical analysis or justifications of literature review, reports of clinical research trials, or fields note. Then new ideas or hypotheses or suggestions will arise and clearly label them as such trials for education and prevention are the ultimate keys to extending good health globally [1],[2], [3], [4], [7], [8], [9], [10], [11], [12], [13], [14], [15], [16], [17], [18], [20], [21], [22], [23], [24], [26], [27], [63], [64], [65], [66], [67].

3. RESULTS

3.1. TOXICITY TEST ON MORTALITY

The biomedicines; Cina 30C and Cina 200C, at extremely low doses, had no direct toxic effects on nematodes mortality respectively.

3.2. ANALYSIS OF RESIDUES TOXICITY

Mulberry leaves collected fifteen days after the last pretreatment, did not contain any toxic residue of the ultrahigh diluted biomedicines; Cina 30C and Cina 200C.

3.3. ROOT-KNOT DISEASE

Table1 shows the pretreatment effects of ultra-high diluted biomedicines; Cina 30C and Cina 200C, at an extremely low doses, on M. incognita pathogens infected mulberry plants in a field trial replicated thrice (P<0.01 by 't'- test).

3.4. FOLIAR DISEASES

Table 2 shows the pretreatment effects of the ultra-high diluted biomedicines; Cina 30C and Cina 200C, at an extremely low doses, on leaf spot, powdery mildew, mosaic viral and tukra diseases of mulberry plants in a field trial replicated thrice assessed initially (Day- 0) and after a period of 30 days (Day -30) by 't'- test (P<0.01). Both; Cina 30C and Cina 200C, with pretreatment significantly reduced the number of leaves infected with leaf spot, powdery mildew, mosaic viral, and tukra (Plate 3) as compared to the untreated condition (Day- 0). The percentage of control achieved in both drugs respectively; were 60.12%- and 62.08%- for leaf spot, 76.88%- and 77.89%- for powdery mildew (Plate 4), 64.15%- and 64.91%- for mosaic virus (Plate 5), 36.32%- and 38.42%- for tukra infection as compared to the untreated level (Day- 0). In the case of infected untreated plots leaf spot, powdery mildew, mosaic viral and tukra diseases showed naturally 27.80 %, 17.76 %, 29.37 %, and 21.20 % reduction respectively, in 30 days (Day -30).

3.5. EFFECTS ON FEEDING SILKWORMS

Table 3 shows the pretreatment effects of the ultra-high diluted biomedicines; Cina 30C and Cina 200C, at an extremely low doses, on diseased infected mulberry plants in a silkworm rearing and field trial replicated thrice on the feeding, growth, and mortality of silkworms (P<0.01 by 't'-test). The average consumption of leaves by the 5th instars (Plate 6), the average number of feeding to cocoon formation (Plate 7), the average number of feeding day to cocoon formation, the average number of escaping– feeding during molting and average molting span days were less for the both; Cina 30C and Cina 200C, -pretreated plants than for infected-untreated (control) ones.

3.6. EFFECTS ON SILK PRODUCTION AND REARING PRACTICES

Table 4 shows the effects of feeding the ultra-high diluted biomedicines; Cina 30C and Cina 200C, at an extremely low dose, -pretreated mulberry leaves on silk production, spinning characters, and rearing practices in a silkworm rearing (Plate 7) and field trial replicated thrice (P<0.01 by 't'-test).

3.7. FUTURE SUGGESTIONS IN RESEARCH

Here, the results fulfill the goal of a research idea because the present pretreatments with the ultra-high diluted biomedicines; Cina 30C and Cina 200C, at an extremely low dose, need to justify future research.

3.8. SCIENCE AND TECHNOLOGY COMMUNICATION GREEN ECONOMY APPLICATIONS

Achieved by; campaign, aware, discuss, arrange workshops and seminars, make news, and publish as abstract regarding the importance of "Pretreatment with the ultra-high diluted; Cina 30C and Cina 200C, at an extremely low doses".

4. **DISCUSSION**

4.1. ON PRESENT STUDY

4.2. ON PLANT DISEASES

The ultra-high diluted biomedicines; Cina 30C and Cina 200C, at an extremely low doses, ones again not only reduced root-knot, leaf spot, powdery mildew, viral, and tukra diseases but also improved the nutritive value (especially protein) of the pretreated leaves of the naturally infected plants [5], [6], [7], [8], [9], [10], [11], [12], [13], [14], [15], [16], [17], [18], [25].

4.3. ON SILK PRODUCTION

Both, biomedicines; Cina 30C and Cina 200C, -pretreatments directly influences on the consumption of leaves, number of feeding, and number of feeding day to cocoon formation, and indirectly effects on molting stage in the infected treated groups from this trial. And due to the ill development of infected untreated (control) batches, silkworm larvae took more time to molt which is proved from the number of escaping feeding during molting. Higher nutritive value especially protein of treated plants contributed to higher growth of silkworm larvae, silk gland weight, cocoon weight, and shell weight which increase silk production significantly for commercial purposes [5], [6], [7], [8], [9], [10], [11], [12], [13], [14], [15], [16], [17], [18], [25].

4.4. ON GREEN ECONOMY

The improved health of the larvae, cocoon weight, silk gland, and shell weight from both the biomedicines; Cina 30C and Cina 200 C,-pretreated groups of infected plants might have resulted in the fewer starting time to spinning and span of spinning day and the total elimination of the mortality rate respectively. Or, both the biomedicines; Cina 30C and Cina 200 C,- might have infused into mulberry leaves a substance that has conferred disease resistance on growing silkworm larvae by releasing defense-related natural products by plants [2], [3], [4], [5], [6], [7], [8], [9], [10], [11], [12], [13], [14], [15], [16], [17], [18], [20], [21], [22], [23], [24], [24], [25], [28], [34], [51], [52], [59], [68], [69]. For this, the effective rate of rearing (ERR%) is very high in all; Cina 30C and Cina 200C, -pretreated-treatment-batches which enriches the sericulture industry in many ways, especially for commercial purposes as well as green economy.

4.5. ON TOXICITY

The present study clearly showed that the ultra-highly diluted drugs; Cina 30C and Cina 200C, were pretreated as effective or potential biomedicine at extremely low doses and it had no direct toxic effect on plants but to the pathogens of mulberry plants larvae [2], [3], [4], [5], [6], [7], [8], [9], [10], [11], [12], [13], [14], [15], [16], [17], [18], [20], [21], [22], [23], [24], [24], [25], [28], [34], [51], [52], [59], [68], [69].

4.6. ON SYNTHESIS

Both the Cina 30C and Cina 200C could induce synthesis of some antagonistic substances in the pretreated plants. Lectins accumulated in gall regions of root of *Hibiscus esculentus* infected with *M. incognita* [2], [3], [4], [5], [6], [7], [8], [9], [10], [11], [12], [13], [14], [15], [16], [17], [18], [20], [21], [22], [23], [24], [24], [25], [28], [34], [51], [52], [59], [68], [69], [70].

4.7. ON DISEASE RESISTANCE MECHANISMS

Systemic acquired resistance can be induced by in different crop plants by localized virus infection, non-pathogenic and pathogenic microorganisms, or their culture filtrates or by salicylic acid [2], [3], [4], [5], [6], [7], [8], [9], [10], [11], [12], [13], [14], [15], [16], [17], [18], [20], [21], [22], [23], [24], [24], [25] [28], [34], [51], [52], [59], [68], [69], [70], [71], [72], [73] or by the polar vesicl74 or by the defense-related triterpene glycoside avenaacin A-1 is synthesized [75].

4.8. ON DEFENSE RESPONSE

It is reported that a plant plasma membrane ATP binding cassette-type transporter is involved in antifungal terpenoid, for this transporter in disease resistance76-77 or by the share of common antigens with its host plants77 or by the pure compounds of acaciasides [2], [3], [4], [8], [13], [14], [15], [16], [17], [18], [20], [21], [22], [24], [25], [34], [52], [78], [81].

4.9. ON PATHOGENESIS RELATED PROTEINS

The ultra-highly diluted drugs; Cina 30C and Cina 200C, may synthesis various antigens particularly (low molecular weight proteins; 5kd to 25kd) and induce defense responses involving several pathogenesis-related proteins in which the naturally infected plant pathogens fail to tolerate [2], [3], [4], [5], [6], [7], [8], [9], [10], [11], [12], [13], [14], [15], [16], [17], [18], [20], [21], [22], [23], [24], [25], [28], [34], [51], [52], [59], [68], [69], like the NE (nematode extract) [3], [82], [83].

4.10. ON BIODIVERSITY

Those showed that nematode pathogens infestation somehow serves as a repressor for the expression of defense gene in plant [2], [3], [7], [8], [9], [10], [11], [12], [13], [14], [15], [16], [17], [18], [20], [21], [22], [24], [25], [34], [51], [52], [82], which can be assumed with pretreated-biomedical drugs; Cina 30C and Cina 200C, at an extremely low dose, serve as a stimulus for the expression of many new induced defense-related PR-proteins by systemic acquired resistance.

4.11. NOW THE KEY QUESTION

Is, whether plant-derived natural products, the ultra-highly-diluted pretreated- drugs; Cina 30C and Cina 200C, at an extremely low dose, can be used as potential biomedical by inducing defense-response against various plant-pathogens causing major mulberry-diseases in a field trial and silkworms rearing [2], [3], [7], [8], [9], [10], [11], [12], [13], [14], [15], [16], [17], [18], '[20], [21], [22], [24], [25], [34], [51], [52], [82], [83].

4.12. NOW THE KEY ANSWER

Is, the ultra-high-diluted-pretreated-biomedicines; Cina 30C and Cina 200C, at an extremely low dose, was not only highly effective in ameliorating different mulberry diseases but also enriched sericulture industry as well as green agriculture economy. And it is also noted that pretreatment with, the biomedicines; Cina MT and Cina 30C and Cina 200C, at an extremely low dose, and *A. nilagirica*- extracts or *A. auriculifirmis*-extracts, at an extremely low dose, show more or less same results [5], [7], [11], [12], [14], [15], [22], [25].

4.13. FOR FUTURE RESEARCH

4.14. IN GENOME BIOLOGY

We're not completely human, at least when it comes to the genetic material inside our cells; 145-genes from bacteria, other unicellular organisms, and viruses with 17- as possible horizontal gene transfers [84], the genomic sequencing 96.2% identical to a bat coronavirus and shares a 79.5% sequence identity to SARS-CoV [84], [85], [86], deal with the structure and function of genetic material underpinning all organisms [85], [86], [87], [88]. Approximately, ten percent of the human genome is made of bits of virus- DNA [89]. Human endogenous retroviruses are by far the most common virus-derived sequences in the human genome90 which don't always require a body [91].

4.15. IN GENETIC RESISTANCE

It is reported that genetic resistance to coronavirus infection according to those three host resistance mechanisms: genetic control [44] and SARS-CoV-2 is the etiological agent responsible for the pandemic COVID-19 outbreak and the main protease (Mpro) of SARS-CoV-2 is a key enzyme that plays an important role in helping in viral replication and transcription-structure-based design of antiviral drug candidates targeting the SARS-CoV-2 main protease [92].

4.16. IN IMMUNE SYSTEM BLUEPRINT

Once the virus infects the host cell, it takes over the host cell's machinery to produce more viruses. The host cell essentially becomes a virus factory. When the human body is attacked by germs, the immune system kicks into gear to fight, by improving the immune system, creates a blueprint of the attacking agent, by which, the body effectively remembers the germ - enabling a person to fight for re-infection by the same or similar viruses [93].

4.17. TRADITIONAL MEDICINE IN HUMAN HISTORY

In the evolution of human history shows the people are using traditional medicine for therapeutic purposes, and the 70%- 80% population is primarily dependent on animals and plant-based [37], [46].

4.18. THERAPEUTIC VALUE OF TRADITIONAL MEDICINES

It is reported that the 'Indian wormwood'- *Artemisia nilagirica*, is considered against many ailments as it is possessed to have high content of biologically active molecules and essential oils. It has been used since centuries in antimicrobial, antifungal, antibacterial, and filarial, insecticidal, antiulcer, anticancer, antioxidant, anti-proliferative, healing potential, neurological disorders, tuberous sclerosis, dermal infection, larvicidal, anti-inflammatory activities, anti-asthmatic and anti-malarial activity, Parkinson's disease, Alzheimer's disease, hypertension, diabetes, atherosclerosis, cardiovascular diseases, cytotoxic, malignancy, genetic abnormalities, diabetes, epilepsy, asthma, sychoneurosis, depression, anxiety and stress, leucorrhoea, threatened abortion, hemoptysis, tuberous sclerosis, skin diseases, immunological disorders, and the aging process, and the pharmacological studies confirm its therapeutic value due to the presences of the wide range of chemical compounds which indicate that the plant could

serve as a potent material for the development of novel agents having good efficacy in various disorders in the coming years [54], [55]. It is used for the treatment of human parasites, animals, and plants. The common photochemical of *A. nilagirica* that causes effective results on human health care biologically active chemical compounds are flavonoids, alkaloids, tannins, glycosides, phenol, saponins, terpenes, amino acids, quinines, phlobatannins and volatile oils, polysaccharides, sesquiterpene lactones, coumarins and acetylenes, and terpenoids [54], [55], [56], [57], [58]. Forty-three constituents (98.16% essential oil); 79.91% monoterpenoids and 18.25% sesquiterpenoids, α-Thujone (36.35%), β-thujone (9.37%), germacrene D (6.32%), 4-terpineol (6.31%), βcarvophyllene (5.43%), camphene (5.47%) and borneol (4.12%), were the major constituents from aerial parts of Artemisia nilagirica [94]. The Artemisia has a diverse range of activities for medicinal uses in human and plant diseases ailments due to possess several active constituents that work through several modes of action and the 1, 8cineole, beta-pinene, thujone, artemisia ketone, camphor, caryophyllene, camphene and germacrene D are the major components in most of the essential oils of this plant species [95]. Artemisia has long been not only used in traditional medicine and but also as a food source for different functions in eastern Asia [96]. Its essential oils has hepatoprotective- and hepatic non-toxic- effects, and as a natural source of hepatoprotective agent96. But, 4th May 2020, WHO recognizes that Artemisia annua are being considered as possible treatments for COVID-19 and should be tested for efficacy and adverse side effects? [97].

4.19. THERAPEUTIC APPROACH

Recently, the NovavaxInc, which contributed to the development of other epidemic vaccines, has announced it is currently in pre-clinical animal trials for several multiple nanoparticle COVID-19 vaccine candidates, by using their recombinant protein, the adjuvant is 'saponin-based' and it has shown a "potent and well-tolerated effect" [98], [99]. Scientists are trying to discover novel inhibitor molecules against enzymes Mproand ACE2 by the use of phytochemicals, which be utilized for further innovation and development of antiviral compounds against Coronavirus [100].

4.20. VACCINATION

So, for successful vaccination requires four components. Human Immunomics Initiative (HII) aims to decode the underlying mechanisms and rules of how the human immune system fights disease with advances in computing and artificial intelligence, genomics, systems biology, and bioinformatics101. And should follow the guideline of WHO entitled "Vaccine-preventable diseases and vaccines" [37], [101], [102]. It reduces wait time for emergency vaccination [105] and one or more randomized trials will be needed to answer¹⁰⁶. Then, with allopath is using trial and error method in some cases to treat COVID-19 [97], [107] and according to the World Health Organization's latest table of COVID-19 vaccines, 124-candidates with technologies or platforms. Merck's new investments focus on two different COVID-19 vaccines that are already in early clinical trials [108].

4.21. DEVELOPMENT OF IDEAS FOR EMERGENCY VACCINATION

In this situation, it will be essential to inform public health expertise for moving academic research forward during COVID-19, and a gradual, stepwise approach to reopening [109]. And, the present results and discussion fulfill the goal for the research suggestions because the present pretreatments with the ultra-high diluted biomedicines; - Cina MT or – Cina 30C and Cina 200C- liquid or - Cina 30C and Cina 200C- globules, at an extremely low doses, prepared from the flowering meristem of *A. nilagirica*, mixed with water at an extremely low dose, need to justify future research [5], [7], [11], [12], [14], [15], [16], [18], [22], [25], [33], [60], [97].

4.22. IDEAS FOR EMERGENCY VACCINATION

Perhaps no country is more vulnerable to COVID-19's depredations than Yemen which was grappling with "the largest humanitarian crisis in the world¹¹⁰. So, we urgently need effective drugs for coronavirus disease 2019 (Covid-19), but what is the quickest way to find them¹¹¹? For this, apply the plasma from COVID-19 survivors to help save others [112]. Recently, the Max Planck Institute test *Artemisia annua* plant extract [97], [113] against the novel

coronavirus disease (COVID-19 and *A. annua* extracts show very little toxicity and artemisinin-based drugs are widely used to treat malaria even in newborns [113]. So, I think, though it is maybe applicable as a vaccine, but it will not be cost-effective and affects biodiversity in conservation with green economy applications [5], [7], [11], [12], [14], [15], [16], [18], [22], [25], [33], [60], [114]. Hence, biomedicines, Cina MT [97], [113] may be used in vaccine formulations to regulate immune function by acting as -antioxidants and -scavenge oxidative stress^{5,7,11-16,18,22,25,33,6097,113} due to the presence of chief constituents of many human health care potential biologically active chemical compounds. that work through several modes of action; are flavonoids, alkaloids, tannins, glycosides, phenol, saponins, terpenes, amino acids, quinines, phlorotannins, polysaccharides, sesquiterpene lactones, coumarins, acetylenes, and volatile oils; terpenoids, monoterpenoids, sesquiterpenoids, α -Thujone, β -thujone, betapinene, germacrene D, 4-terpineol, β -caryophyllene, 1, 8-cineole, artemisia ketone, camphor, caryophyllene, camphene, and borneol etc., - isolated from the crude extract of *A. nilagirica* flowering meristem [54], [55], [56], [57], [58], [94], [95], [96], [97].

4.23. IDEA-I:

So, the adjuvant Cina MT [97], [113] may be used with recombinant protein nanoparticle antigens derived from the coronavirus spike protein and combine these antigens with its adjuvant Cina MT for the final formulation of the vaccine and it may be shown a "potent and well-tolerated effect" through stimulating the entry of antigen-presenting cells into the injection site and enhancing antigen presentation in local lymph nodes, boosting immune responses [5], [7], [11], [12], [14], [15], [16], [18], [22], [25], [33], [60], [98], [99], [114]. In a letter as an e-mail, the Science Advisory Board Net, at Express Cells, for their business of creating better knock-in cell lines for drug discovery, toxicology, and other biologic research and add for purchase SARS-CoV-2 Spike Protein [115] and the readily available coronavirus spike proteins may be helped to use for vaccine preparation which may fight against "COVID Toes among kids [116], which gain immunity before the onset of disease or disease symptoms in an individual as a prevention rather than cure [117] and in a clinical study shows the efficiency of triple antibiotic mixture process in immature apex [117], [118]. It is obligatory that information on Clinical Trials.gov, a resource provided by the U.S. National Library of Medicine (NLM), to the National Institutes of Health (NIH) or other agencies of the U.S. Federal Government, is provided by study sponsors and investigators, and they are responsible for ensuring that the studies follow all applicable laws and regulations [116], [117], [118], [119], [120], [121]. It is also studied the costeffectiveness of emergency care interventions in low and middle-income countries like India [117], [118], [119], [120]. But it will not also be; -cost-effective and not easily -prepare able, -available and -not help in green economy applications [5], [7], [11], [12], [14], [15], [16], [18], [22], [25], [33], [60], [97], [113].

4.24. IDEA-II

The adjuvant biomedicines, Cina MT^{97,113} may be used with anti-Human antibodies like IgG (A80-104A, A80-105A), IgM (A80-100A, A80-101A), & IgA (A80-102A, A80-103A) and offer treatments or vaccine preparation of COVID-19 (SARS-CoV-2) and it may also be accelerated the discovery to improve lives [101], [116], [117], [118], [119], [120], [121], [122]. After getting successful clinical trials, the concerned authorities, may be permitted for the use as a vaccine for treatments [101], [116], [117], [118], [119], [120], [121]. But it will not also be; -cost-effective and not easily -prepare able, -available and -not help in green economy applications [5], [7], [11], [12], [14], [15], [16], [18], [22], [25], [33], [60].

4.25. IDEA-III OR IDEA-IV

The ultra-high diluted biomedicines; –Cina 30C liquid OR -Cina 200C liquid, @ 10 drops mixed with 10 ml of sterile distilled- or pure drinking -water, maybe orally administered once daily (before taking any food) for 15 days, against naturally occurring virus infections15-days before symptom onset OR illness onset (as a vaccine) OR onset of symptoms where patients in hospital-associated COVID-19 infections has been reported (treatments) [123], [124]. In the case of treatment, depending on the disease intensity, the dose may be increased 3-4 times a day. It is moderately cost-effective and easily -prepare able and –available drug [117], [118], [119], [120]. After getting

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permission from the concerned authorities, the Cina 30C OR -Cina 200C -liquid, may be directly used for "Clinical trial or as a Vaccine" because ultra-high diluted biomedicine -Cina 30C OR -Cina 200C -liquid, have actually no drug molecules (due to cross the Avogadro number i.e., 6.023 X 1023) [101], [116], [117], [118], [119], [124], [125]. It is well known that Avogadro limit washed out by nano-associates of water which continue as information carriers in serial dilutions and end up with the generalized concept of medicines and these structures, in their turn, influence near-matching bio-molecules to serve as medicines, like antibiotics, leading to a generalized concept of medicine [120], [121]. It may be more; cost-effective [117], [118], [119], [120], easily prepare able, easily available, easily applicable and help in green economy applications also [5], [7], [11], [12], [14], [15], [16], [18], [22], [25], [33], [60], [97], [113].

4.26. IDEA-V OR IDEA-VI

The ultra-high diluted biomedicine globules; –Cina 30C OR -Cina 200C, @ 10- medicated- globules (7.2mg), maybe orally administered once daily for 15 days, against naturally occurring virus infections 15-days before symptom onset OR illness onset (as a vaccine) OR onset of symptoms where patients admitted in hospital with COVID-19 infections has been reported (treatments) [120]. In the case of treatment, depending on the disease intensity, the dose may also be increased 3-4 times a day. It is the most cost-effective and easy -prepare able and – available drug [117]. The biomedicine globules; –Cina 30C OR -Cina 200C, may also be directly used for "Clinical trial or as a Vaccine" after getting permission from the; -WHO, -ClinicalTrials.gov., -U.S. NLM and -NIH [101], [116], [117], [118], [119], [124], [125]. It is the most; cost-effective, easily prepare able, easily available, and help in biodiversity conservations and green economy applications issues [5], [7], [11], [12], [14], [15], [16], [18], [22], [25], [33], [60] and easily applicable also [97], [113].

Recently, scientists in Israel, Netherlands claim progress in COVID-19 monoclonal antibody— 47D11 trials [126] and Italy claims to develop first COVID-19 vaccine¹²⁷. India applied the very old theory for vaccine preparations and plasma therapy is being treated as yet another complementary treatment to help the COVID-19 patients recover [127]. The current pandemic locust attack in India causes the crises of food securities [128], the world has joined hands to find a vaccine for the novel coronavirus. At present, many groups (80) are working globally for vaccines for humans which normally takes years to develop. Currently, there are¹¹¹ potential vaccines for the SARS-CoV-2 which are in different stages of clinical trials [127].

While a cure or vaccine for COVID-19 is not available, in the absence of any side-effects and adverse interactions with any conventional medicines along with a robust safety profile and repeated evidence-based successes against viral infections, the ultra-high diluted biomedicine; -Cina MT or -Cina 30C liquid or -Cina 30C globules, at an extremely low dose, may play an important role in the fight against COVID-19¹²³. It is the most; cost-effective, easily prepare able, easily available, and help in biodiversity conservations and green economy applications issues also [5], [7], [11], [12], [14], [15], [16], [18], [22], [25], [33], [60] and should be applicable for clinical trials as early as possible [97], [113].

Now it is planned to publish six-ideas for current outcomes and therapies on coronavirus disease (COVID-19) outbreak that helps the readers as well as a scientific community to take measures or treatment opportunities or discovery of vaccines to avoid new coronavirus.

5. Conclusions

It can be concluded that the plant-derived natural products, ultra-high-diluted cost-effective, easily applicable, pretreated-ecofriendly easily available drugs; Cina, at an extremely low dose, used as a potential biomedical drug by inducing defense- response against various pathogens causing major mulberry diseases and the "Six Ideas; for vaccine and clinical trials with the ultra-high diluted biomedicines; Cina MT OR Cina 30C liquid OR Cina 200C liquid OR Cina 30C globules OR Cina 200C globules, at an extremely low dose, against COVID-19 by boosting the immune system for the Improvement of Science and Technology Communication Green Economy Applications Issues" and the future clinical-scientists develop all aspects of clinical-case-reports globally with the sincere hope that this crisis will soon be over and the whole world may retain in normal forms by fighting against COVID-19 war.



Plate 1: Flowering meristem of Artemisia nilagirica (Clarke) pamp



Plate- 2. Field grown with mulberry plants naturally infected with M. incognita.



Plate- 3. Mulberry leaf infected with 'Tukra disease'.



Plate- 4. Mulberry leaf infected with 'Powdery mildew'.



Plate- 5. Mulberry leaf infected with 'Mosaic Virus'.



Plate- 6. 5th instar larvae of Bombyx mori L.



Plate-7. Cocoon formation by 5th instar larvae.

Table 1: Effects of pretreatment with the ultra-high-diluted biomedicines; Cina 30C- and Cina 200C- at an extremely low dose, on root-knot diseases, *Meloidogyne incognita* infected mulberry plants in a field trial replicated thrice.

	thrice													
Pretreat	Average No.		Average		Average Protein content				Average Nematode			Averag	ge No.	
ment	of		Surface area of		(%) +				population +			of		
batches	leaves/plan		leaves									rootgalls/pl		
(20plants t*		(sq.cm)*		Leaf Root				Soil (200g)		Root (2g)		ant +		
/plots &	Day-0	Day-	Day-0	Day-30	Day-	Day-	Day-	Day-	Day-0	Day-	Day-0	Day-	Day-0	Day-
8		30			0	30	0	30		30		30		30
plots/														
batches)														
*	260	400	5605	0454	0.00		1.0.0	5 .00	1005	501	(00	105	1105	004
Infected	360	420	7685	2451	2.98	6.75	4.38	7.82	1937	78b	639	107	1197	221
Pretreate	ax	by	ax	6by	ax	by	ax	by	ax	У	ax	by	ax	by
d	±12.	±13.	±157.	±408.	±0.1	±0.2	±0.1	±0.3	±74.	±3.	±24.	±5.0	±46.	±8.5
(Control)	67	43	70	60	3	5	6	0	50	39	57	9	03	0
Infected	362	424	7683	2521	2.99	6.78	4.38	7.88	1935	66c	639	55d	1207	187
Cina	ax	by	ax	7dy	ax	by	ax	су	ax	у	ax	у	ax	су
30C-	±12.	10.1	±143.	±387.	± 0.1	±0.2	±0.1	±0.2	±74.	±2.	±22.	±2.3	±46.	±6.6
Pretreate	83	2±	30	91	2	4	5	6	30	35	03	9	42	7
d														
Infected	360	426	7682	2521	2.99	6.78	4.38	7.89	1933	62c	639	54d	1208	184
Cina	ax	by	ax	5dy	ax	by	ax	су	ax	У	ax	У	ax	су
200C-	±12.	12.1	±143.	±327.	±0.8	±0.1	± 0.1	±0.2	±74.	±2.	±22.	±2.3	±40.	±6.6
Pretreate	83	2±	30	02		2	5	2	34	32	03	2	42	4
d														

'*' - means average values of 40 plants in triplicate.

'+' - means average values of 20 samples in triplicate.

'Day-0' - means before pretreatment.

'Day-30' - means after pretreatment.

'a,b'- significant difference by t-test (P<0.01) in the same column.

'x,y'- significant difference by t-test (P<0.01) in the same row between day-0 and day-30 of each character.

Table 2: Effects of pretreatment with ultra-high-diluted biomedicines; Cina 30C- and Cina 200C- at an extremely Low dose, on leaf spot, powdery mildew, mosaic and tukra diseases of mulberry plants in a field replicated thrice assessed initially (Dav-0) and after a period of 30 days (Dav-30)

replicated tillice assessed initially (Day-0) and after a period of 50 days (Day-50)									
Pretreatment	Average number of disease-infected leaves / plant (%)								
groups	Leaf spot		Powdery mildew		Mosaic		Tukra		
(20 plants/									
Plot & 8	Day-0	Day-30	Day-0	Day-30	Day-0	Day-30	Day-0	Day-30	
plots/group)	-	_	-	-	-	-	-	-	
Infected	70.58ax	98.38ay	80.75ax	98.51ay	68.68ax	98.05ay	57.15ax	78.35ay	
Pretreated	±2.28	±3.93	±3.23	±3.94	±2.74	±4.10	±2.38	±3.26	
(Control)		(<27.80%)		(<17.76%)		(<29.37%)		(<21.20%)	
Infected Cina30C -	70.55ax	10.43by	80.87ax	3.99by	68.36ax	4.21by	57.01ax	20.69by	
Pretreated	±2.31	±2.11	±3.01	± 0.01	±2.42	±0.13	±2.07	±0.11	
		(>60.12%)		(>76.88%)		(>64.15%)		(>36.32%)	
Infected Cina 200C	70.53ax	8.45by	80.86ax	2.97by	68.32ax	3.41by	57.11ax	18.69by	
-Pretreated	±2.71	±2.71	±3.11	± 0.01	±2.62	±0.13	±2.37	±0.81	
		(>62.08%)		(>77.89%)		(>64.91%)		(>38.42%)	

Day-0 means before pretreatment.

Day-30 means after pretreatment.

a,b- Significant difference by 't'-test (P<0.01) in the same column.

x,y- Significant difference by 't'- test (P<0.01) in the same row between day-0 and day-30 of each character.

()- Figures in the parentheses show percentage of reduction on day-30 as compared to the initial level on day-0 in the same row.

Table 3: Pretreatment effects of disease-infected and ultra-high-diluted biomedicines; Cina 30C- and Cina200C-pretreated at an extremely low dose, mulberry plants in a field on the feeding and growth of silkworm in the
silkworms rearing trials (replicated thrice)

Treatment	Average number of									
batches	Consumption	Feeding to	Feeding-	Escaping	Moulting	Larval fresh	Mortality			
(180 larvae/	of leaves(g)	cocoon	day to	feeding	span day	weight (g)	rate (%)*			
batch)*	(5 th instar)*	formation	cocoon	during	$(1^{st} to 5^{th})$	(5 th instar)*+				
		*	formation	moulting*	instar)*					
			*							
Infected	4.03a	76.00a	19.00a	51.00a	13.00a	1.48a	56.00			
Pretreated	±0.15	±2.37	± 0.50	±1.75	±0.39	±0.03	±2.43			
(Control)										
Infected	2.46b	62.00b	15.00b	20.00b	5.00b	2.63b	Nil			
Cina 30C -	±0.09	±1.93	± 0.44	±0.68	±0.15	±0.06				
Pretreated										
Infected	2.42b	60.00b	15.00b	20.00b	5.00b	2.61b	Nil			
Cina 200C	± 0.04	±1.92	± 0.40	±0.62	±0.13	± 0.05				
-Pretreated										

a,b- different small letters in a column show significant difference by 't'- test (P<0.01).

* - average values of 180 silk worm larvae in triplicate.

+ - average values of 10 silk worm larvae were dissected in triplicate.

Table 4: Pretreatment effects of disease-infected, and ultra-high-diluted biomedicines; Cina 30C- and Cina 200C

 pretreated at an extremely low dose, mulberry plants in a field on the growth of silk gland, spinning time, cocoon,

 shell, rearing, sex ratio and egg laying capacity in the silkworms rearing trials (replicated thrice)

	Average								
Pretreatment	Silk gland	Starting	Span of	Cocoon	Shell	Shell	Effective	Sex ratio	Egg
batches	fresh	time to	spinning	fresh	fresh	ratio	rate of	(Male /	laying
(180 larvae/	weight(g)	spinning	day *	weight	weight	(SR%)	rearing	Female%)	capasity
batch)*	(5 th	(at day-		(g)*	(g) +	+	(ERR%)*		
	instar)+)*							
Infected	0.98a	34.00a	10.00a	0.85a	0.11a	12.94a	21.37a	76.00a	320.00a
Pretreated	±0.03	±1.30	±0.45	±0.03	±0.01	±0.49	±0.63	±1.94	±13.91
(Control)									
Infected	1.98b	20.00b	3.00b	1.09b	0.24b	22.01b	97.43b	68.00b	540.00b
Cina 30C	± 0.07	±0.51	±0.09	±0.04	±0.02	±0.67	±2.16	±1.74	±11.73
-Pretreated									
Infected	1.98b	20.00b	3.00b	1.09b	0.24b	22.01b	97.48b	68.00b	540.00b
Cina 200C	± 0.04	±0.42	±0.06	±0.02	±0.01	±0.42	±2.16	±1.72	±11.71
-Pretreated									

a,b- different small letters in a column show significant difference by 't'- test (P<0.01).

* - average values of 180 silk worm larvae in triplicate.

+ - average values of 10 silk worm larvae and cocoon were dissected in triplicate.

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CONFLICT OF INTEREST

The author have declared that no competing interests exist.

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