COVID-19 LITERATURE DATA ANALYSIS, CURRENT DATA AND MEDICINAL PLANTS (Case of Morocco) – Review Article –

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ABSTRACT

By analyzing the literature since the onset of the epidemic, many scientific articles have appeared on the outbreak, according to the World Health Organization, the disease Covid-19 has been characterized as a pandemic [1]. It seems to have started in December 2019 when the first cases of unknown cause pneumonia were detected in Wuhan (Hubei, China) [2,3]. The results of numerous studies have shown that protease inhibitors and compound, which constitute the major part of the derivatives of Moroccan medicinal plants, can therefore be very effective in controlling the infection induced by the virus. This review was carried out in the hope of helping the public to recognize and deal effectively with the new coronavirus in 2019 (SARS-CoV-2), and to provide a reference for future studies.

Keywords: Covid-19, SARS-CoV2, coronavirus, Chloroquine, Hydroxychloroquine, The Remdesivir, medicinal plants, Morocco.

No : of Figures : 05  
No : of References : 41
INTRODUCTION

Since the end of December 2019 a new epidemic Covid-19 appeared and shocked the world, the epidemic is of a bream-COV2 virus.

These events are accompanied by an explosion of information and clinical and epidemiological research. This outbreak has been detected in several countries of the world first appeared in China late 2019. This led to a rapid epidemic of a new strain of coronavirus called SARS-CoV-2, which means coronavirus of severe acute respiratory syndrome 2. Associated disease, now called Covid-19, spread rapidly in mainland China and in China. The rest of the world with countries like South Korea, Iran and Italy particularly affected especially Italy has known a rapid spread of the virus.

The corona virus affects 213 countries (Figure1,2) world wide, has contaminated more than:1,789,403 people and 1,09,765 patients died because of the disease. The situation is however better in China, where the number of new people infected with coronavirus almost does not increase for several days. In Wuhan, the authorities alleviate the rules of Confinement after two strict months without outputs. In total, 245,855 patients are cured of the disease in the world since the beginning of the pandemic[1]. Europe has become the epicenter of the epidemic. The countries most affected by the coronaviruses are Italy with over 152,271 confirmed cases and 19468 deaths from the disease are cured and 32534 die (Figure1,2). A figure that is rising again after a slight drop the previous day. Spain, where the situation is deteriorating a little more each day, more than 166 019 people tested positive Covid-19 and 16972 deaths in April 12 2020[1].

In many countries, the authorities have improved the health measures and, in some cases, restricted travel and large gatherings of people, in Morocco there was a landing of intense security, and by order of His Majesty King Mohammed VI, and the closure mosques this decision was never taken before in the history of Islam in order to limit the spread of the virus and prevent hospital overload: in Morocco the cases confirmed up to April 12 are: 1617, deaths 113 and healings 153.
Figure 1: COVID-19 pandemic statistics on the evening of 04/12/2020 in Morocco

Figure 2: Statistical COVID-19 pandemic in the evening 04/12/2020
All continents have reported confirmed cases of Covid-19. Africa has confirmed its first case in Egypt 14 February 2020. China is the largest trading partner of Africa; well, there are large volumes of travel through which the coronavirus 2 of SARS could reach the mainland. Early detection of importing Covid-19 and the prevention of further transmission are crucial challenges for all import risk countries from areas with active transmission in China. 12 countries in Asia, Europe and North America have already reported secondary spread after importation[4]. Algeria, Ethiopia, South Africa and Nigeria were among the 13 priority countries identified by the WHO on the basis of their direct links and volume of their trips to China. The import risk to African countries is very heterogeneous, Egypt, Algeria, South Africa, Ethiopia and Nigeria being the most exposed. The first case of Covid-19 x declared in Morocco March 2, 2020 confirmed the pastor institute flap of a Moroccan national living in Italy the patient benefit from the follow-up unit of the isolation hospital Moulay Youssuf Casablanca or it is supported by the health measures in force[5].

What is a coronavirus (SARS-COV2) and Transmission:

Regarding research on pandemic Ncov 2019-to date, show that the genome (GenBank accession MN908947 ) Has the highest similarity (89%) with an associated member of the SARS Sarbecovirus (GenBank accession MG772933 ). A sub-genre of the genre β coronavirus [6].

Figure 3: COVID-19 pandemic statistics at 04/12/2020
The preliminary genome sequence suggested that the snake was probably a wildlife reservoir responsible for the current epidemic of infection Covid-19 and identified unknown homologous recombination in advanced glycoprotein Covid-19 which could explain the transmission inter-species of snake man [7], rodents and various wild animals [8]. However, this theory has now been largely discarded and some researchers refer bats as a reservoir and doubt that the coronavirus may have come from animals other than birds and mammals [7].

The new coronavirus incubation period is estimated between 7 and 14 days. The symptoms are similar to other respiratory viruses, including fever, cough and shortness of breath with radiographs showing invasive lesions in the lungs. Some cases require hospitalization due to worsening of the clinical condition and in many cases, complications can lead to death [9,10,11].

The transmission and close contact are the most common modes of transmission for SARS-CoV-2. Aerosol transmission could also be a means of transmission. In addition, the researchers also detected SARS-CoV-2 in samples of stools, gastrointestinal tract, saliva and urine. On the bioinformatic database, the data indicate that the gut could be a potential route of infection with SARS-CoV-2[12]. Consistently, the RNA of SARS-CoV-2 was also detected in gastrointestinal tissue Covid-19 patients[13]. In addition, SARS-CoV-2 was detected in tears and conjunctival secretions Covid-19 patients[14]. Meanwhile, a retrospective study based on nine Covid-19 pregnant women had reached for the first time indicated that the possibility of Intetrauterine vertical transmission between mothers and infants in late pregnancy was temporarily excluded [15]. However, available data on pregnant women infected with SARS-CoV-2 was insufficient and, therefore, further studies are needed to verify the potential vertical transmission of SARS-CoV-2 in pregnant women.

Tang and his colleagues drew readers' attention to the emergence of Covid-19 and reported that pregnant women were also susceptible to SARS-CoV-2. Clinical manifestations of Covid-19 pregnant patients in this study varied widely from asymptomatic to severe, similar to the previous report in non-pregnant patients[16]. Previous studies have suggested that Covid-19 is more likely to affect older men with comorbidities [17].

**Treatment Covid-19**

For the treatment of this pandemic several clinical trials have been proposed but until the day there is no effective treatment for healing the sick of Covid-19.

**Treatment by immunotherapy with antibody-based**

The therapeutic design in a time accelerated using antiviral existing treatment that has shown promising results against MERS and SARS. more detailed understanding of the virus pathogenesis could increase the specific therapeutic product design opportunities [18].
The need to address the new emerging coronavirus that causes global impact highlights the development of passive immunotherapy monoclonal antibody-based to provide a response. Even if there is a major advance toward developing a therapy monoclonal antibodies to coronavirus, no monoclonal antibody has yet been successfully commercialized. The growing understanding of MERS-CoV and SARS-CoV in recent years could galvanize the community research will make significant progress in the Covid-199 and the therapeutic design in an accelerated time using the existing antiviral regimen that has shown promising results against MERS and SARS. Thorough understanding of the virus.[18].

The convalescent plasma or immunoglobulins were used as a last resort to improve the survival rate of SARS patients whose condition has continued to deteriorate despite treatment with pulsed methylprednisolone. In addition, several studies have shown a shorter hospital stay and lower mortality in patients treated with convalescent plasma than those who were not treated with convalescent plasma in 2014[19, 20, 21].

Evidence shows that the convalescent plasma from patients who have recovered from viral infections can be used as a treatment without occurrence of side effects serious events. Therefore, it might be useful to test the safety and effectiveness of convalescent plasma transfusion patients infected with SARS-CoV-2.

**Chloroquine and hydroxychloroquine against coronavirus**

Chloroquine is an amine acidotrope form of quinine was synthesized in Germany by Bayer in 1934 and appeared there about 70 years as an effective substance of natural quinine derived from plant endemic South American (the Cinchona) [22,23].

Hydroxychloroquine was as active as chloroquine against malaria Plasmodium falciparum and less toxic, but is much less active than chloroquine against P. falciparum chloroquine-resistant because of its physicochemical properties. Which is advantageous with hydroxychloroquine is that it can be used in high doses for long periods with very good tolerance. Unfortunately, the efficacy of chloroquine has gradually decreased due to the continued emergence of P. falciparum resistant to chloroquine[24].

Chloroquine has proved capable of inhibiting in vitro the replication of several coronaviruses. Recent publications support the hypothesis that chloroquine can improve clinical outcomes of patients infected with SARS-CoV-2. Multiple molecular mechanisms by which chloroquine can achieve these results remain to be explored. Since the SARS-CoV-2 was discovered a few days ago as the same cell surface receptor ACE2 (expressed in the lungs, heart, kidneys and intestines) that SARS-CoV-1 [25,26,27].

SARS-COV2, like other human coronaviruses, include three envelope proteins, spike (S) protein (180-220 kDa), membrane (M) protein (25-35 kDa) and
envelope protein (E) (10-12 kDa), which are required for the entry of infectious virions in the target cells. The virion also contains the nucleocapsid (N), capable of binding to the viral genomic RNA, and nsP3, a key component of the replicase complex. A subset of β-coronavirus uses a hemagglutinin in-esterase (65 kDa) that binds the sialic acids on the surface of glycoproteins. The S glycoprotein determines the host tropism. It seems that SARS-CoV-2 binds to the enzyme conversion of angiotensin 2 (ACE2) expressed on pneumocytes [25,28]. The binding to ACE2 should trigger conformational changes in the S glycoprotein allowing cleavage by transmembrane protease TMPRSS2 protein S and the release of S fragments in the cell supernatant that inhibit virus neutralization by antibodies[29]. The virus is then transported into the cell through early endosomes and late wherein the protease B cathepsin L cleaves more protein S at low pH, resulting in the fusion of the viral envelope and the phospholipid membrane of endosomes resulting in the release of viral genome into the cell cytoplasm. Replication begins and viral genomic positive strand RNA is transcribed into a negative RNA strand that is used as a template for synthesis of viral mRNA. The synthesis of
the negative RNA strand rises earlier and faster fall than the synthesis of the positive strand. Infected cells contain between 10 and 100 times more positive than negative strands strands. The ribosomal machinery of infected cells is diverted in favor of the virus. After replication, envelope proteins are translated and inserted into the endoplasmic reticulum and then move to the Golgi compartment. The viral genomic RNA is packaged in the nucleocapsid and the envelope proteins are incorporated during the step of budding to form mature virions. The M protein, which localizes to the trans-Golgi network, plays an essential role in viral assembly by interacting with other proteins of the virus. After assembly, the newly formed viral particles are transported to the cell surface in vesicles and are released by exocytosis. It is possible that chloroquine interferes with the glycosylation of ACE2 receptor, thereby preventing binding of SARS-CoV-2 to target cells. Chloroquine may also limit the biosynthesis of sialic acids that may be required for binding to the cell surface of SARS-CoV-2. If the binding of certain viral particles is reached, chloroquine can modulate the acidification of the endosomes, thereby inhibiting the formation of autophagosome. Thanks to the reduction of kinase cell activation by mitogen activated protein (MAP), chloroquine can also inhibit virus replication. Also, chloroquine may alter the maturation of M proteins and interfere with the assembly and budding of virions. Regarding the effect of chloroquine on the immune system, see the elegant review Savarino et al. Chloroquine could alter the maturation of M proteins and interfere with the assembly and budding of virions. Regarding the effect of chloroquine on the immune system, see the elegant review Savarino et al. 

The use of chloroquine in Morocco for the treatment of Covid-19

The use of chloroquine and articles published about the properties of this molecule in the treatment of cases of aggravated Covid-19-ill patients in several scientific journals, a number of countries such as China[7] or the United States and France[32] all confirmed positive results for the use of this protocol in the treatment of Covid-19, confirmed Wednesday, March 25, 2020, the Ministry of the Moroccan Health[7].

The Moroccan Ministry of Health highlights have adopted this treatment protocol after a review and the decision of the Technical and Scientific Committee of the National Program for Prevention and control of influenza and severe acute respiratory infections. Thus declared in a statement that the description and use of this medicine, which he generalized the administration in university hospital center (CHU) and the Regional Directorates of Health in the territory of the Kingdom, will treat cases of Covid-19-ill patients[7].

The Remdesivir against coronavirus

The first patient infected with SARS-CoV-2 was treated with supportive care and
remdesivir intravenously before the patient recovers and is released)[33]. Here, we review the literature on existing antiviral agent but not approved, the remdesivir, which has a promising antiviral activity in vitro and preliminary clinical experience in the treatment of Covid-19. Although SARS-CoV and SARS-CoV-2 share only 82% of RNA sequence identity, their RNA-dependent RNA polymerase (RdRp) shares 96% sequence identity[11]. Therefore, drugs targeting viral proteins of SARS-CoV RdRp may be effective for SARS-CoV-2. For RdRp target gender β-coronavirus, there are several potential drugs or compounds, including favipiravir, ribavirin, penciclovir, galidesivir the remdesivir, analogs of the 6’-fluorinated aristeromycin and analogs acyclovir Fleximer®[12]. Remdesivir (GS-5734), the phosphoramidate prodrug of a nucleoside adenosine C[13] Has a structure similar to that of tenofovir alafenamide, which is a nucleotide analogue of adenosine 5-monophosphate having antiviral activity against hepatitis B and HIV (HIV). It was developed by Gilead Science Inc. and has not been authorized or approved to date. In addition, the GS-441 524 was recommended for the treatment of cats with feline infectious peritonitis, which is rare but fatal and is caused by a feline coronavirus[34].

With an effective reduced lung viral load in a murine model of infection with SARS-CoV, a potent antiviral activity against SARS-CoV-2, an acceptable safety profile of treatment remdesivir parenterally in two reports of case, and a randomized trial of the Ebola disease, the clinical use of remdesivir in cases of Covid-19 is expected. Two randomized clinical trials on the treatment remdesivir parenterally in the treatment of Covid-19 in China could open the way for an effective antiviral treatment for such epidemic infectious disease[35]. Two multicenter clinical trials phase 3, randomized, double-blind, placebo-controlled are underway in China.

Traditional Chinese Medicine to fight against coronavirus

In 2003, patients of severe acute respiratory syndrome (SARS) treated with TCM (Traditional Chinese Medicine) benefited from a shorter hospital stay, reduced side effects associated with steroids and improvement in symptoms[36]. In particular, the genomic characterization and new coronavirus has revealed that he is closely related to the SARS coronavirus, suggesting further that MTC could have potential use in the current outbreak[37].

Indeed, the Chinese government advised doctors to consider combining with Western antiviral TCM remedies to fight against the new coronavirus pneumonia. However, there were few studies to help select the appropriate herbal medicines before biological experiments and expensive clinical trials.

Medicinal plants, especially those used in traditional Chinese medicine, have attracted considerable attention as they contain bioactive compounds that could be used to develop formal drug against several diseases with zero or minimal side effects[38]. A comprehensive library of medicinal plants containing 32,297 potential antiviral phytochemicals and traditional
Chinese medicinal compounds were generated from data and studies collected by a group of researchers\cite{37,38,39,40,41} and analyzed in relation to SARS-CoV2. Compounds of medicinal plants are already used to successfully treat many viral diseases. Database analysis planned drugs on medicinal plants containing 32,297 phytochemicals antiviral potential this group of researchers concluded that these plants awaken likely results of inhibiting the activity of the SARS-CoV-2 3CL pr (Viral enzyme 3 chymotrypsin-like cysteine protease) control the replication of coronaviruses and thus viral replication. Other in vitro assays and in vivo are needed to turn these tested in clinical trials anticipated that information obtained in this study could be useful to explore and develop new therapeutic agents natural anti-Covid-19 the future.

Traditional Medicine in Morocco and COVID-19

Morocco, physiographic and bioclimatic diversity is a variable explanatory of the richness and floristic diversity especially in terms of plants Medicinal and Aromatic PAM. Medicinal flora is widely used by populations who have know-how in terms of its use, culture and conservation. In Indeed, most rural populations use PAM as a remedy for their health, and use them in cosmetology, perfumery, food..., Currently, herbal medicines can provide us with solutions concerning the constraints linked to health, especially in developing countries and why not for the new disease and pandemic at COVID-19. The lack of drugs or a vaccine against the coronavirus makes some people play sorcerer’s apprentices. Whether in Morocco or in other countries, people are turning to aromatic and medicinal plants to stem their pandemic in their own way. Indeed, Morocco ranks second in the world after Turkey in terms of plant diversity. In addition, this plant wealth includes more than 42,000 varieties of plants, including around 800 varieties with specific aromatic and medicinal properties. We have selected previous studies that have been done on PAM and that have approved that these plants can play an antiviral activity.

Several studies on phytotherapy have shown that the Moroccan flora is rich in terms of antiviral activity as shown in the following table:
Zineb et al.,

**Figure.5: Moroccan Medicinal and Aromatic Plants with antiviral activities.**

<table>
<thead>
<tr>
<th>Vernacular name of the plant</th>
<th>Scientific name</th>
<th>Active ingredient (majority compounds)</th>
<th>Pharmacological properties</th>
<th>References</th>
</tr>
</thead>
<tbody>
<tr>
<td>Er-râs</td>
<td><em>Calendula officinalis</em> L.</td>
<td>Carotenoids and xanthophylls (0.017 to 0.078%), Flavonoids (0.88% in the petals, 0.33% in the inflorescences), triterpene glycoside, Polysaccharides (15%)</td>
<td>Antibacterial, Antiviral and Antioxidant, Anti-inflammatory, Immunostimulant</td>
<td>K. Ghédira and P. Goetz, Calendula officinalis L. (Asteraceae) : souci,” <em>Phytotherapie</em>, 2016 vol. 14, No. 1, p. 1–6. <a href="https://doi.org/10.1007/s10298-016-1022-y">https://doi.org/10.1007/s10298-016-1022-y</a></td>
</tr>
<tr>
<td>Iwîza</td>
<td><em>Lippia citriodora</em></td>
<td>citronellal (14.40%), isogeraniol (6.40%),</td>
<td>Antibacterial, Antifungal</td>
<td>Zineb Jalal, Yassine el Atki and al, Phytochemistry of the essential oil of Melissa officinalis L. growing wild in Morocco: Preventive approach against nosocomial</td>
</tr>
</tbody>
</table>

**Er-râs**

- **Carotenoids and xanthophylls (0.017 to 0.078%)**
- **Flavonoids (0.88% in the petals, 0.33% in the inflorescences)**
- **Triterpene glycoside**
- **Polysaccharides (15%)**

**Pharmacological properties**

- Antibacterial
- Antiviral
- Antioxidant
- Antiproliferator
- Anti-inflammatory
- Immunostimulant
<table>
<thead>
<tr>
<th>Species</th>
<th>Plant Name</th>
<th>Constituents</th>
<th>Activity</th>
</tr>
</thead>
<tbody>
<tr>
<td>Habaq el-bahr</td>
<td><em>Mentha longifolia</em> (L.) Huds</td>
<td>Oxygenated monoterpenes (80.5%)</td>
<td>Antimicrobial</td>
</tr>
<tr>
<td>Za’tar</td>
<td><em>Origanum compactum</em> Benth</td>
<td>1<em>Thymol (10.33%), Carvacrol (43.58%), γ-Terpinene (8.71%) et p-Cymene (18.58%)</em></td>
<td>Antiviral, antibacterial and antioxidant</td>
</tr>
<tr>
<td>Qronfel</td>
<td>Syzygium aromaticum (L.)</td>
<td>Eugenol (75.0-88.0%) flavonoid and tannins</td>
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<tr>
<td></td>
<td></td>
<td>1. Antiviral, antibacterial Pest control, immunostimulant</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>2. Anti-nociceptive and Anti-inflammatory</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Skenjabil</th>
<th>Zingiber officinale</th>
<th>Gingerol (15%).</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Antiviral Anti-inflammatory Antioxidant</td>
<td></td>
</tr>
</tbody>
</table>

- **Zingiber officinale**
  - Gingerol (15%).
  - Antiviral
  - Anti-inflammatory
  - Antioxidant

- **Syzygium aromaticum (L.)**
  - Eugenol (75.0-88.0%)
  - Flavonoid and tannins
  - Antiviral, antibacterial
  - Pest control, immunostimulant
  - Anti-nociceptive and Anti-inflammatory

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<table>
<thead>
<tr>
<th>Region</th>
<th>Plant Name</th>
<th>Chemical Component</th>
<th>Antioxidant</th>
<th>Antiviral</th>
<th>Antifungal</th>
<th>Cytotoxic</th>
</tr>
</thead>
<tbody>
<tr>
<td>Azîr, yazîr</td>
<td>Rosmarinus officinalis</td>
<td>verbenone</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Qarfa al-hârra</td>
<td>Cinnamomum verum</td>
<td>methylhydroxy chalcone polymer</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Šîba</td>
<td>Artemisia arborescens</td>
<td>β-thujone (56.33%)</td>
<td>Antiviral</td>
<td></td>
<td>Antifungal</td>
<td>Bacteriostatic</td>
</tr>
<tr>
<td>Kemmûm, īkammen</td>
<td>Cuminum</td>
<td></td>
<td></td>
<td></td>
<td></td>
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</tr>
</tbody>
</table>

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<table>
<thead>
<tr>
<th>Plant</th>
<th>Monoterpene Oxygen and Cinnam Aldehyde</th>
<th>Antimicrobial Antioxidant</th>
<th>Chemical and biological characteristics of <em>Cuminum cyminum</em> and <em>Rosmarinus officinalis</em> essential oils. <em>Food Chemistry</em>, 2007, vol. 102, p. 898-904</th>
</tr>
</thead>
</table>

https://doi.org/10.1002/cbdv.200890045
Conclusion

The COVID-19 epidemic has become a clinical threat to the general population and healthcare professionals around the world. The initial experience of the current pandemic and the lessons from the previous two pandemics can help improve preparedness plans future and to fight the progression of the disease. However, knowledge about this new virus remains limited. The effective option of antiviral therapy and vaccination is currently being assessed and development. What we can do now is implement it in a way aggressive infection control measures to prevent the spread of SARS-CoV-2 by human-to-human transmission. Public health authorities should continue to monitor the situation, because the more we will know about this new virus and its associated outbreaks, the better we can react.

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