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Ellagic Acid Vrs Covid -19 : Functional Food to Drug Discovery

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Abstract

Functional Foods (FF) are historical & cultural. Technologically the shortest, safest & most economic starting material for drug discovery. *In-Silico* studies are computational; multi-disciplinary versatile computational platforms to pre-view anti-body vrs anti-gen interactions and intra-compound compatibility, etc.; validates FFs.Ellagic acid (EA) comprises FF as in PunicaGranatum (peel-pulp-&-juice). Computation is used to evaluate EA as a possible RBD docking candidate of relevance vis-à-vis COV-2 spp. Indicates excellent docking.Good docking means antagonistic. EA is compared with anti-cancer *Simeprevir* (which is re-purposed use in Covid having docking affinity of – 8.52 Kcal/Mol). EA is observed to make very close call (-6.17 Kcal/Mol) with better indicators in all other parameters. Punica Granatum contains (posits) Attractive.Original, Ground breaking.Opportunity full.

Keywords
Ellagic acid; Functional Food; Simeprevir; Covid-19; In-Silico; Antagonistic; Synergic; Multi-Disciplinary.

Introduction

The focus for combating CoV-2 spp., virus has thus far been heavily loaded in favor of vaccines. Internal medicine (orals) and family physicians have been discounted. Pan globally there are dozens of vaccines. Each provides prophylaxis of the order 8-10 months. Post the initial intra-muscular inoculation the native has to take boosters on year on basis. And there are news galore of re-infections during the inoculation and

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the booster dose window and even post the 1st booster. Too many anti-cancer drugs are being repurposed. Thus, there is a case for (orals) clinical diagnosis at presentation; dispensation by the family physicians and consequent therapies cum supportive prescription. And this is due. Drug discovery is time taking; expensive and requires multi-disciplinary brain storming. Hence, 'Bottom Up' models are ideal which in turn is yeomanly facilitated by *In-silico* data which is multi-disciplinary. Behera, et.al.,[1] have done such an (re-purposing i.e., possible off label use) exercise with 56 clinically used compounds and *Simeprevir* transpired as the champion. Bhattacharya et.al., [2] have reported the clinical results of Ellagic acid (EA) on a C-RAD 5 adult anabolic case (encouraging result) which is now on WHO Covid-19 Reseach Database . Ellagic Acid (EA) is the principal constituent in Pomegranate fruit (funtional food candidte). Vis-à-vis Covid-19 and various maladies including of virus etiologies a historiography of EA & pomegranate as a research moiety; as a starting material for drug discovery; as a 'functional food'; etc., for the period 30 years before present is noted[3]. Our clinical understanding of the Covid-19 pathophysiology is partly available in [4-6]. In humans the (sole) receptor-binding domain (RBD) of SARS-CoV-2 is the angiotensin-converting enzyme 2 (ACE2). In this communication we make docking studies of EA against ACE2). And whereas, vis-à-vis CoV-2, EA has thus far not been the candidate of any known *in-sillico* study. Nor has EA been compared on such tool (Auto Dock) against any Gold Standard (namely *Simeprevir*). Auto-Dock 4.2 tool and related computational tools are used. *Simeprevir* is assumed as the Bench mark re-purposed candidate and EA is compared & contrasted with it. This is a nascent ground breaking study and is neither exhaustive nor conclusive.

Docking exercise posits EA as effective vis-à-vis CoV-2 pathophisology. EA transpires as antagonistic. We are inclined to comment EA as a 'functional food' at the least as concurrent to conventional therapies and as a fixed dose medicament based on case specific atypicalities (by the clinician) and also as a possible 'starting material' in drug discovery; etc. Some light is thrown onto EA as a safe & nice candidate for brain storming by stake holders in situations pandemic & yyndemic[7].

Materials and Methods

Structure Retrieval Of SARS COV-2

The experimental receptor-binding domain (RBD) structure of SARS-CoV-2 (CoV-2) was retrieved from the Research Collaboratory for Structural Bioinformatics (RCSB), PDB having id- 6M0J with 2.45 A^0 (angstrom) resolutions. The crystal structure of RBD was found with human angiotensin-converting enzyme 2 (ACE2 attached). Using BIOVIA Discovery studio Visualiser 2019 version, the ACE2 receptor was removed thus yielding the pure RBD crystal for our objectives of docking with EA.

Binding Sites Finding The RBD

RBD plays the vital role in interaction of COVID-19 virus with ACE2 of the human physiology. We have searched the molecular interacting residues of RBD and identified the binding sites of RBD for our study [8].

Retrieval ofstructure of Ellagic Acid

The structure of the EA was downloaded from PubChem database[9]. We searched the EA in PubChem database and downloaded its 3D-structure in 'standard file format' (SDF). Then using BIOVIA Discovery studio Visualiser 2019 version we converted the SDF structure of EA to .pdb format and saved it.

Molecular Docking Study Using Autodock 4.2 Tool

For molecular docking study AutoDock4 tool has been used. It is designed to predict the protein interactions with small molecules that make drugs and substrates. It analyzes the interactions of ligand molecules at the specified target site of the protein structure. We docked EA with RBD using such tool. From

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such docking exercise we got binding energy; ligand efficiency; and inhibition constant. The docking complex was further studied through computational tools to study the intermolecular Hydrogen bonds and the average distance between the bonds.

Effect of Ellagic Acid and Simeprevir on Ace2 Receptor of Human

In this investigation we performed a molecular docking study of EA and Simpreprevir with ACE2 receptor of Human CoV-2.

Comparative Study Of Ellagic Acid With Other Reported Drugs Used Against Sars-Cov-2

(i) Efficacy of EA against the SARS-Cov-2, depending upon its docking results and its interaction with the residues of RBD

(ii) Topicalcorelationing based compare & contrast of EA with a select few of the 56 commercially available drugs for CoV-2 clinical use [see Ref-1; Data not shown]. .

Results

Binding Sites of RBD

From literature survey and crystal structure of RBD-ACE2 complex it is noted that the residues of RBD namely Lys417, Gly446, Tyr446,Tyr455, Ile472,Phe486,Asn487, Tyr489,Gln493, Gly496, Thr500, Asn501, Gly502 and Tyr505 mainly interact with the ACE2 of the human cells during entry into the cytoplasm.

About Ellagic Acid and Simeprevir Structure

From PubChem Database, we obtained the SDF format file of the EA and Simeprevir. Using BIOVIA Discovery studio Visualiser 2019 version we converted it into .pdb file format. EA is a compound with PubChemid 5281855, molecular formula $C_{14}H_6O_8$,molecular weight 302.19 g/mol and with Canonical SMILES ID - C1=C2C3=C(C(=C1O)O)OC(=O)C4=CC(=C(C(=C43)OC2=O)O)O. Figure .1 (A & B) shows the 2D and the 3D-structure of EA. Simeprevir is a compound having PubChem id 24873435, molecular formula $C_{38}H_{47}N_5O_7S_2$, molecular weight 749.9 g/mol and with Canonical SMILES IDCC1=C(C=CC2=C1N=C(C=C2OC3CC4C(C3)C(=O)N(CCCCC=CC5CC5(NC4=O)C(=O)NS(=O)(=O)C6CC6)C) C7=NC(=CS7)C(C)C)OC. Figure 2 (A & B) shows the 2D and the 3D-structure of Simeprevir. Table 1 shows the comparative chemical composition of EA and Simeprevir. Figure 3 is the graphical representation of EA and Simeprevir basing upon their compositional atomic numbers. The blue line (series 1) in graph is for EA and the brown line (series 2) represents Simeprevir.

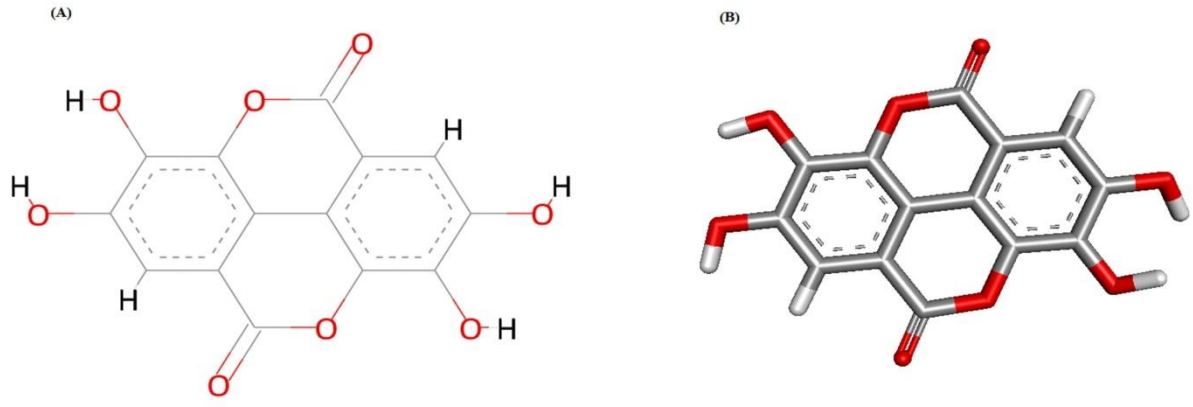

Figure 1: (A) 2D-Structure of Ellagic Acid (B) 3D-Structure of Ellagic Acid

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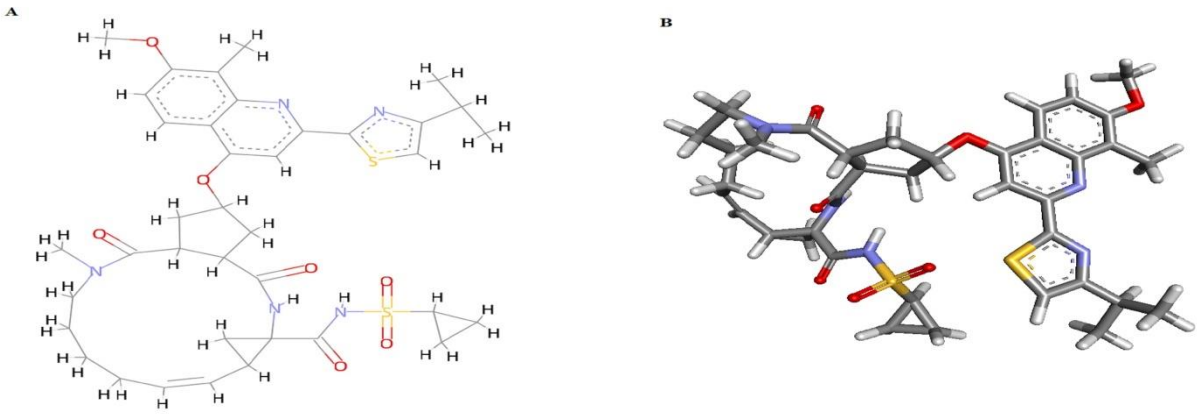

Figure 2: (A) 2D-Structure of Simeprevir (B) 3D-Structure of Simeprevir

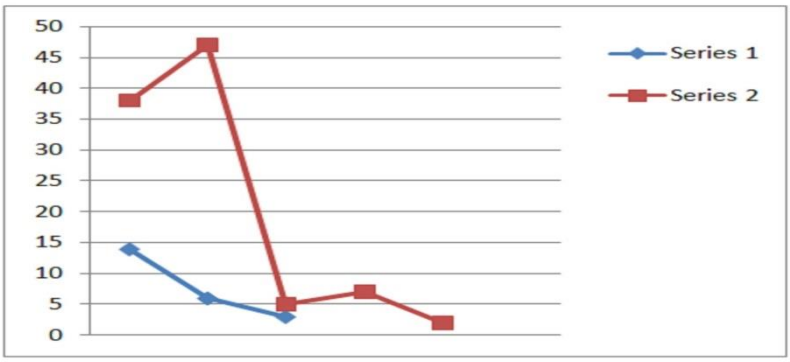

Figure 3: Graphical representation of Ellagic acid and Simeprevir basing upon their compositional atomic numbers. Blue line (series 1) represents Ellagic acid. Brown line (series 2) represents Simeprevir.

Table 1: Results for ellagic acid and simeprevir

Compound	Composition	Series
Ellagic Acid	$C_{14}H_6O_8$	1
Simeprevir	$C_{38}H_{47}N_5O_7S_2$	2

There is deep contrast between the two, yet are complementing & synergistic on the in-silico& all other computational platforms. Thus is a case of Humpty-Dumpty; *Sigmund Freud* 'Compensation Theory/mechanism' i.e., a large & heavier compound benefiting from a small one; not confabulating not contradicting. Relevant in drug designing and in clinical dispensations. Simeprevir having EA as an anomer is theorised to be a stable & physiologically compatible excellent Intra-venous. **Fig-3** gives the Graphical presentation for appreciation.

ADMET Property Checking of Ellagic Acid

- Targetnet web server (http://targetnet.scbdd.com/home/index/)
- ProTox-II web server (https://tox-new.charite.de/protox_II/)

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TargetNet web server is a standard platform to study the Lipinski's rule of 5 and ProTox-II web server is used to study the toxicity of any compound. In order to check the absorption, distribution, metabolism, excretion, and toxicity (ADMET) properties of EA we have used TargetNet server and ProTox- II web server. Table 2 shows the results for TargetNet server (i.e., Lipinski's rule of 5). From ProTox-II server it was found that EA is non-toxic (data not shown). Pharmacological in vitro toxicity studies of EA on dermal fibroblasts[10] & also on MRC-5 cells [11] has reported EA as 'Non-Toxic. Our *in sillico* results are in consonance.

Table 2 **p**resents the molecular parameters cum character of EA as a candidate for *in-sillico* study vrs Cov-2. EA (a natural product) is a component of the human & veterinary physiological processes; Simeperavir is not. 4 HBD helps well in establishing the bonding by the ACE-2. 6 HBA1 helps more in establishing the H bond by EA. EA's HBD/HBA ratio of 4/6 offers a better balanced 2 way vestibule for enzyme bonding than Simeperivir (and, 4/6 is a near Fibonacci number; reckon natural). EA is 2.77 times smaller than Simeprivir (molar refractivity) and hence it exerts greater tissue perforation force and also greater cell transvassation property than Simeperavir. Simeperivir exceeds the HBA1 & LogP limits of Lipinski's. EA is well within limits. All thes sums up as more 'likeness' for EA[12].

Table 3 gives the Comparative toxicity using ProTox-II server, Simeprevir is found to be Toxic in nature; EA is not toxic.

Table 2: Results obtained from targetnet server forellagic acid and simeprevir

SL. NO	Phytochemical's Name	MR (Molar Refractivity) (40-130)	Molecular Weight (<=500 D)	HBD-Hydrogen bond donor (<=5)	HBA1-Hydrogen bond acceptors (<=10)	LogP (<=5)	Lipinski rule of five
1.	Ellagic acid	75.31	302.19264	4.0	6.0	1.3128	100.00%
Comparison with Simeprevir the Champion of the 56 market available anti-Covid screened drugs as in Ref.1							
2.	Simeprevir	208.5224	749.93908	2.0	12.0 ↑	6.9925 ↑	25.00%

Table 3: toxicity checking of ellagic acid and simeprevir using Protox-II server

SL.NO	Compound	Tool	TOXIC/NONTOXIC
1.	Ellagic Acid	ProTox-II	Non Toxic
2.	Simeprevir	- Do -	Toxic

Molecular Docking of Ellagic Acid and RBD of SARS-COV-2

In order to perform molecular docking between EA and RBD of SARS-Cov-2 virionAutodock 4.2 tool has been used. From literature survey the binding sites and grid box value required for docking has been identified. The grid box having X-dimension= 60, Y-dimension= 114, Z- dimension= 62, with spacing 0.375 Å and X-centring = -37.872, Y-centring= 28.878 and Z-centring= 2.979. Docking was done within such grid box values. From molecular docking it is found that EA is having a binding affinity of -6.17 Kcal/mol; Ligand efficiency of -0.28 and Inhibition constant of 30.15 µm. The number of Conventional hydrogen bonds is 7 and the H-bond forming residues are TYR453, GLN493, GLY496, GLN498 and TYR449 with average Distance of H-bonds being 2.403112857 Å (this portends quick & better bonding). Table -4. Figure.4 (A and B) gives the 2D and 3D interaction of EA with RBD .

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Note: Simeprevir's Kd is low (due its anomer). This makes it more unstable in enzymatic binding actions. In the gut & gastric cum enteric phases it gets open to more (unpreditable) reactions\interactions and logical gets positioned as contrdictory. H Bond firmity depends upon coulumbic interaction[13]. Electronegativity of the hydrogen atom assist while the positive charged (S) and neutral charge atoms (N) do not [Table-1]. Anthocynins/Gallagic/Benzoic group of drug's are strongly electron negative and their bio-systemic uptake pathways are ionic[14] and is evidenced as para-magnetic in mechanics[15] and electro-negative coulumbic interaction in particular. Thus from coulumbic perspective EA is a better candidate than Simeperavir. EA also is close to Citric acid ($C_6H_8O_7$). And, citrated enzymated reactions leads to super glues & cements[16]. This means nice bonding with consequent efficient-swift-secure innoculation of the virion'scytoplasm.

Table 4 **shows** EA makes a quite close call with Simeprivir. Additionally, is non-toxic and offers many other subtle advantages. It posits as a good synergy providing candidate (in viremia or malignancy or alongside high potency\monoclonal anti body {mab} or target therapy). It also aspects more residue enzymes on the S domain. 'Neutralizing Antibodies' is a neo find cum evidence based concept [17]. Since EA can bind to the RBD of the Covidvirion'sS-domain via the ACE-2 terminal it can as well 'squat' thereupon and thereby thwart pathogenesis i.e., act as versatile 'neutralizing anti-body'. This may be primal cause of anti-inflammatory effect of EA nd of Gallagic group members (logical hypothesis).

Table 4: results of docking of ellagic acid and Sars-Cov-2

Sl. No.	PubChem CID	Drug	Binding Energy(Kcal/Mol)	Ligand Efficiency	Inhibition Constant (µm)	Dis-asssociation Constant (µm)	No. Of H-Bonds	H-Bond Forming Residues	Average Distance Of H-Bonds (Å)
1.	5281855	Ellagic acid	-6.17	-0.28	30.15	11	7	TYR453,GLN493,GLY496, GLN498,TYR449	2.40311 2857 (8 % less ?)
Simeeperavir the Champion of Ref -1									
2.	24873435	Simeprevir	-8.52	-0.16	564.68	Not Known	4	GLN493,SER494	2.81031

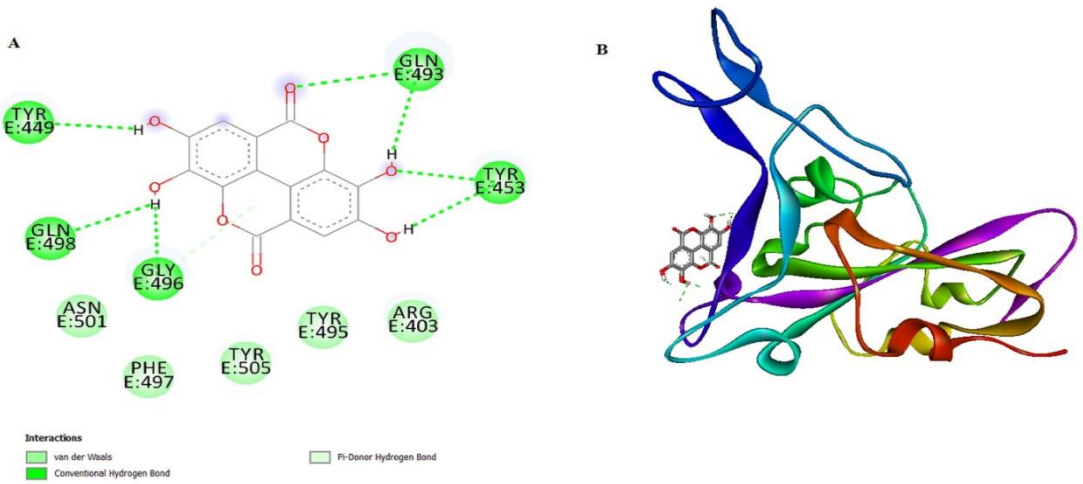

Figure 4: (A) 2D-interaction of Ellagic acid with RBD (B) 3D-interaction of Ellagic acid with RBD.

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Results and Discussion

The lesser known notable aspects of EA vis-à-vis Simeperavirare that Either have an in-blood life off 48hrs. That the inter molecular force (IMF) is more dominant in the case of EA; average distance of H bond is less by an order of 0.4 Å (8% less time); EA has more H bond forming residues (on the S domain) which makes it more versatile and finally has 136% less of heavy atoms. This means EA is more stable in face of stimulus; catalyst or any moderate insult (drug induced & or systemic) whereas Simeprevir can wonder off (due to greater spin of the heavy atoms) also greater in-field in-vivo distraction (blood flow\breathing\peristalsis\etc., offer ever present systemic turbulence during docking moment); Simeperivir($C_{38}H_{47}N_5O_7S_2$) has a lower dissociation constant than EA and hence is toxic & inflammatory & less versatile (possibility of in-gut *N*-nitroso compounds formation looms large). Simeprevircontains Sulfur which under bolus loading dose is rank carcinogenic and in sub-clinical or fractional dose is mutagenic (supporting info) and in-vivo Nitrogen (also in neoplasogenesis) is life, process& activity maintainer cum select up-regulator. Simeprevir's dis-association constant is less. Greater Kd means better stability in gastric & gut phase. Simeprevir has an anomer. And anomers are well known to disassociate when exposed to gastric chamber and in the gut phase (microbiome) of the digestive system (EA does not suffer such disadvantage). EA also scores better as it has more number of H bond forming residues. EA gets full blood borne within 90 minutes (anthocynine/phenolic/Gallagic moieties) being up-taken at mid-gut via the Urolithinpathway;with concurrent microbiom protection Akkermansia muciniphila [18] via Nrf2 pathways [19]; moreover enters the infested cell via the Nf-kB terminal and neutralizes the highlystable vessel damaging crystalline Hemozoin. Interestingly, there is a robust angiotensin-II–NF-κB axis in Covid pathophisiology [20]. Thus concurrent introduction of anthocynine/phenolic/Gallagic moieties may adversely affect the entire RNA cascade i.e., (good or bad) virus replication. EA also has salutary effect on the Akkermansia muciniphila [21]. EA also qualifies the Lipinski's rule better. Simeprevir having EA as an anomer is theorised to be an excellent Intra-venous. Points in the direction, Simeprevir + EA = Humpty Dumpty = marriage of a large compound with a small = synergic compensation = attenuation of dynamics = better yield = combined dynamic drug (CDD).

Fiscal aspect: Simeprevir anti-covid capsule of 150mg potency is administered @ 1 cap daily (adult). The price in hand per cap is at least @ US $50 i.e., per dose per day. EA costs US $ 15 per gm (works out to 3 days medication @ 300mg per day @ 100mg TID post prandial). And, dried rind powder of the chloroplast stage pomegranate contains EA as a non-confounding constituent ~ ready for direct use [22]. Functional foods do fail the Fiscal Affordability Test.

Effect of Ellagic Acid and Simeprevir on ACE2 Receptor

An investigation is made between EA ↔ human ACE2 receptor and again between Simeprevir ↔ human ACE2. This is pan global 1st study. The ACE2 receptor was availed from PDB ID 6M0J, which has been taken for the current investigation. In the structure of 6M0J the human ACE2 receptor is attached with the RBD of SARS-Cov-2. By removing the RBD structure the structure of ACE2 receptor the 6M0J PDB ID was got. Then the structure of Simeprevirwas collected from PubChem database in 3D –form in SDF format. Using BIOVIA Discovery studio 2019 version it was converted into .sdf format. Then, the binding sites of ACE2 receptor were located by using GHECOM web server [23] to predict the binding sites of ACE2 receptors. Thereafter molecular docking study of ACE2 receptor with EA and Simeprevirwas done respectively using Autodock 4.2 tool. The grid box value taken are (X-dimension= 98, Y-dimension= 126 and Z-dimension=76, spacing 0.375 Å with X-center= -24.213,Y-center=17.786 and Z-center= -25.202). Table**.5** presents the results.

Table 5 Shows the results for docking of Ellagic acid and Simeprevir with ACE2 receptor.
Figure 5& 6 shows the results for the interaction of Ellagic acid with ACE2 receptor of Human.

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Figure 7 & 8 shows the results for the interaction of Simeprevir with ACE2 receptor of Human.

Table 5: Docking study of ellagic acid and simeprevir with human ace2 receptor

Sl. No.	PubChem CID	Drug	Binding Energy(Kcal/Mol)	Ligand Efficiency	Inhibition Constant (µm)	No. of H - Bonds	H-Bond Forming Residues	Average Distance of H-Bonds (Å)
1.	5281855	Ellagic Acid	-5.66	-0.26	71.13	5	THR371, CYS361, CYS344, ASP367	2.244138
2.	24873435	Simeprevir	-7.34	-0.14	4.19	1	ARG273	2.91031

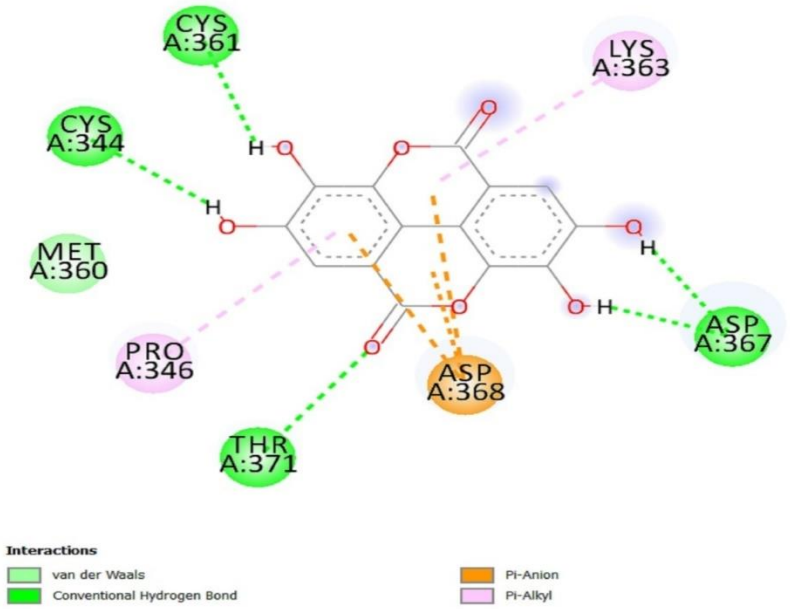

Figure 5: Shows the 2D-interaction of Ellagic acid with ACE2 receptor

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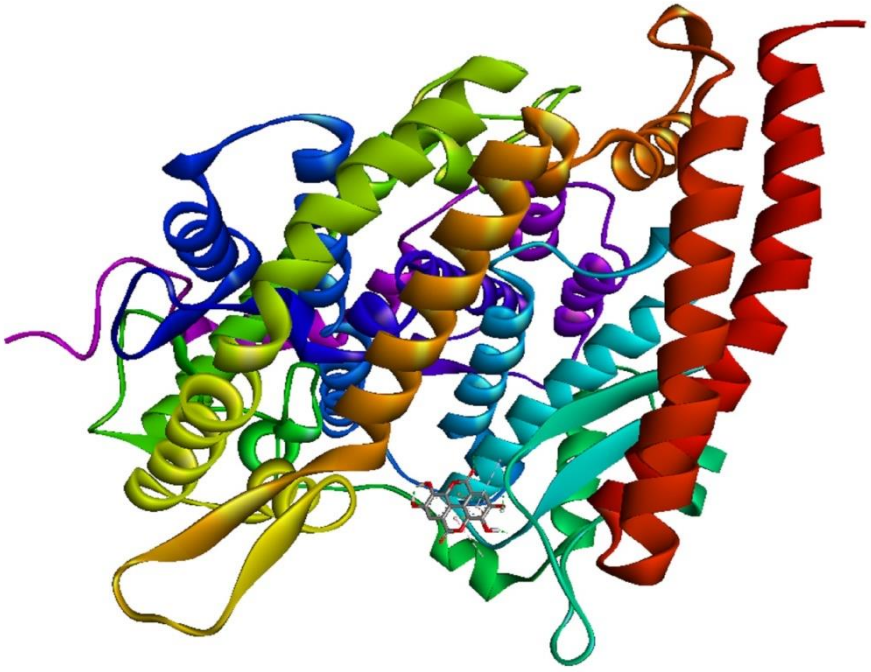

Figure 6: Shows the 3D-interaction of Ellagic acid with ACE2 receptor

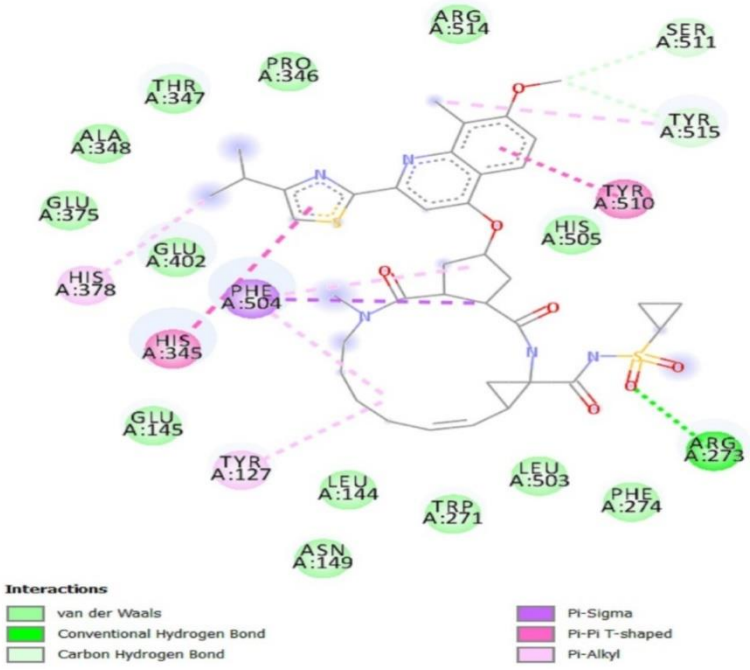

Figure 7: Shows the 2D-interaction of Simeprevir with ACE2 receptor

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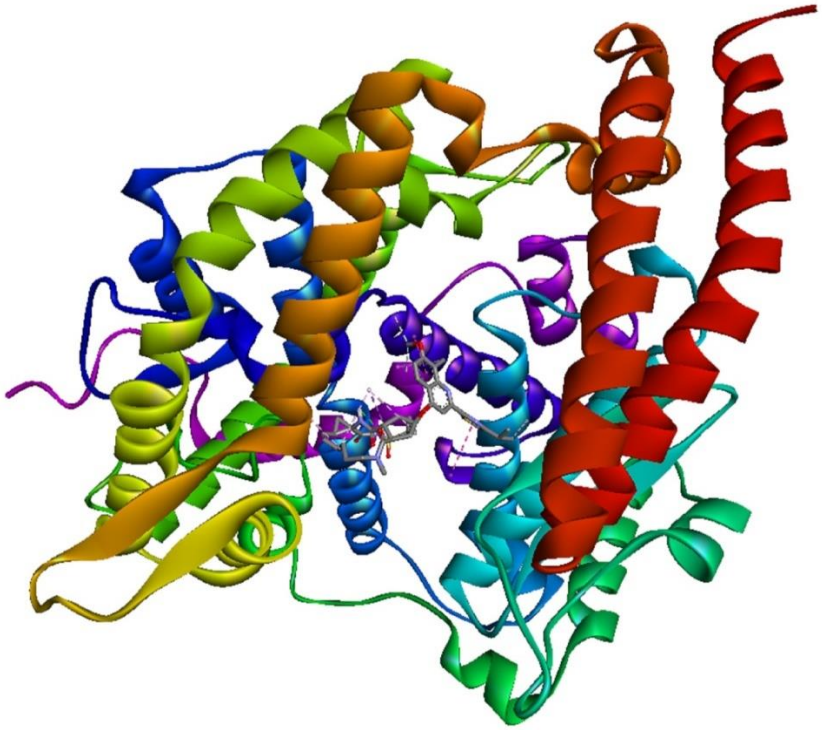

Figure 8: Shows the 3D-interaction of Simeprevir with ACE2 receptor

The Dalton ratio between EA &Simeprevir is of the order 1 : 2.48. Binding energy ratio is of the order 1 : 1.3. The Ki ratio is 17.75 : 1. EA interacts with more number of binding residues and also the H bond distance is less. Thus EA has a better specificity for human ACE-2. Since EA is non-toxic; is anti-inflammatory i.e, apart (synergy & complementing role); good likeness, etc., it can bind to ACE-2 of non infested or infested\infected cells and theoretically can squat on ACE-2 and other receptors and thereby fail a gamut of cell spp., type invading anti-bodies it posits as a versatile 'neutralizing antibody'. This is important from conservative, multi-organ distant metastatic malignancies more specially in 'sentinel nodes' health keeping; liquid cancers; geriatric stage (ever present) innate systemic inflammations & medicine, refractile patient clinical handling perspectives. Moreover, L-threonine = THR*↑ the most efficient H bonding residue enzyme candidate is conspicuous by absence in the Simeprevir –ACE2 bond while EA has it.

Comparative Study of EA With Other Reported Drugs

Herein below EA is compared & categorized with all the 56 drug moieties as in Ref-1 in Table 6, Table 7, Table 8, Table 9, Table 10, Table 11 and Table 12 (Supplementary File). Tables 6-to-12 are provided as auxillary\supplementing files and may be accessed via the 'hyper-link'. When we compare EA with Presatovir, Tiddeglusib, Enzaplatovir, Grazoprevir, Daclatasvir and Dolutegravir it is noted that EA offers less binding affinities and the inhibition constant is also greater. But when we consider H-bonds, EA is found to have comparatively more H-bonds. When we compare Entecavir and Ribavir with 8 H-bonds, it is noted that, they have less binding affinity and high inhibition constant as compared to EA (more obstructive affinitive; pre or post binding {if any} difficulty in disassociation = variable outcome including possibility of mutagenesis and/or intra-compound adverse/un-desirable interaction, etc. And other compounds

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reported have less binding affinities and less H-bonds in comparison to EA (not Tabulated). EA posits as better and suggests synergic use possibility.

Lead Functional Food - EA.

Stone hard dried peel of the juvenile (Chloroplast stage) pomegranate comprises of EA as a neat moiety. Indian classical Ayurveda (exclusively) uses an atypical indo native sub-spp., which is a mini fruit and yields not any sweet juice save & except EA & the harsh ellagi-tannins. Sun drying\shade drying affluxes ethylene and residual alkaloids leaving back EA and ellagitannins (2 or 3 near identical type moieties) only. These tannins on ingestion hydrolyze in the gastric phase (stomach & small intestine) to form EA & tannins (back & forth). Either compound groups are helpful for the systemic Akkermansia muciniphila(gut) envira and whereas on the other hand has adverse effect on non systemiccum pathogenic bio-films [24] . Either effects are via para-magnetic (ionic) mechanism. Furthermore, EA is broad spectrum anti-virus including HIV (this paragraph supporting info; own). Thus pomegranate posits as the choice best (EA containing) Functional Food in caption domain.

Figure 9 is that of the indo-native classical Ayurvedic Dalimba a unique sub species of the *Punica Granatum L*. This(1.5-to-2.5 cm L) is the full mature size. In this image the member of the said fruit has ripen. Even then its juice is harsh. It is not eaten, only used for medicinal; faith & culture based rituals and activities (specially the carp only). The image is that of at ripe stage. Whole rind off the fruit is used; seeds or aril not (*note* : seeds have opposite moieties). It is the choice best natural year longstore house of EA& also of ellagitanins, thus is a unique case of a functional food. Hippocrates of Kos, Greece, (460A.D.)said "Let food be thy medicine and medicine be thy food", i.e., 'functional food' [Well known].

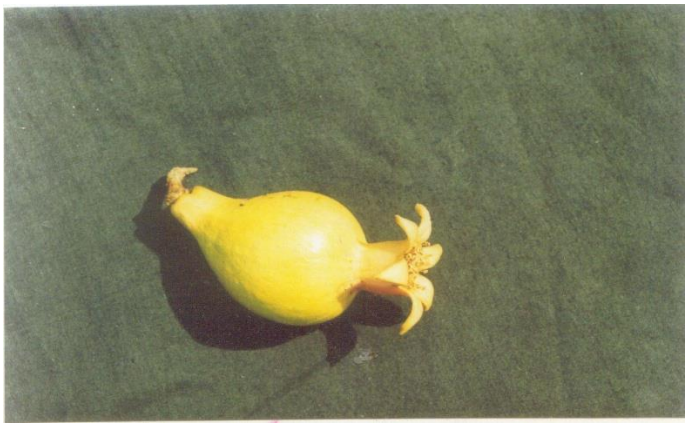

Figure 9: Own exposed image. Ayurvedic Dalimb

This *in-sillico* study indicates that EA the natural compound is fully in consonance with thus far pharmacologically reported wide & good medicinal properties including anti-inflammatory i.e., anti-cytokine storm [24] of EA extracted from various natural/synthetic sources. Against viral outbreak EA containing agro products (e.g., Pomegranate squash) [25-27] and 'AVIR' fixed dose formula [28] based internal medicine are a potent defense weapon in the hands of the Family Physicians for community based family welfare – as 1st stage of intervention at presentation; as 'functional food' alongside conventional therapies and as a versatile tool in the hand of the nurses. EA also offers good scope to be administered as intra

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venous; jointly or severally. Hence, EA posits as a good-to-excellent functional food sourced candidate compound in the search for drugs against SARS-CoV-2 and virus in general. We are encouraged to write this communication (molecular docking validation) as a 'Functional Food' loaded with EA acid (sourced from a fruit) has been uptaken by the WHO in its 'COVID-19 Research Data Base' [29].

Conclusion

EA follows the rules of ADMET properties. Its RBD docking against CoV-2 S pike has better binding affinity with minimal inhibition constant with higher number of H-bonds. Our Tables are quite talkative and transpiration thereof positions EA as an evidence based molecule\compound that can be used in vary many ways viz., (i) starting material in drug discovery (ii) as synergy provider to front line repurposed conventional therapies in 'n' number of pathologies\maladies (iii) down turning of toxicity & innate systemic inflammation and or drug induced (iv) appreciating the frailties of existing repurposed drug moieties (v) specificity as an anti-viral specially against CoV-2 (vi) getting to know the comparative lesser known aspects of drugs; related terms and acronyms by various stake holder groups viz., clinicians; meaning and scope in the literature designed for clinician's education & propaganda (vii) widening the clinician's choice in going for individual case specific approach (vii) evidence based 'functional food' possibility that are rich in bio-similars as supportive/s; (ix) Neutralizing antibody; (x)safety & economies of scale; (xi) ennobles the family physicians; (xii) as a versatile compound for use in 'geriatric medicines'; etc.

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Declaration of Interest

From the society-to the society-for the society. Authors also declared that they have NO conflict of interest; NO financial support (loans or grants of any type or form included); this is not any donor driven program NOR do they have any hidden\underlying commercial OR faith based nexus. Therefore, NO interests in any patents, frank – open.

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