Preprint 56: Parasitic Associations, Antimicrobial Actions, and Bacteriostatic Antibiotics with Cytochrome P450 Inhibitors

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1 Abstract

Carbon, hydrogen, oxygen, nitrogen and sulfur in amounts, arrangements and ratios form an important relationship in the control of bacteria, gene expressions, and protein interactions with DNA/RNA, other proteins and enzymes. There are 40 million bacterial cells in a gram of soil and a million bacterial cells in a millilitre of fresh water with about 5×1030 bacteria on Earth and are vital in many stages of the nutrient cycle by recycling nutrients such as the fixation of nitrogen from the atmosphere. A hydroxycoumarin antibiotic that is obtained from Streptomyces rishiriensis and exhibits potent antibacterial and anticancer activity. For example, 8 compounds have avg values shown in Table 1 are

	CO	HC	NO	CS
1	2.7923	0.01137	0.002214	0.4975
2	2.748	0.1380	0.000263	0.9054
3	1.9168	0.1768	0.0002596	0.2288
4	2.6181	0.06754	0.0003857	0.2024
5	15.377	0.13144	0.0003447	0.2273
6	7.547	0.01129	0.002762	0
7	8.365	0.11660	0.002397	0.2718
8	2.377	0.13008	0.0005422	0.2579

For (1) diferuloylmethane, (2) 4, 5, 7,-trihydroxyflavone, (3) Glycyrrhiza glabra, (4) guggulsterone, (5) Thymoquinone, (6) Silibinin, (7) Scutellarin and (8) Quercetin, Ursolic acid, 3, 5, 4 -trihydroxy-trans-stilbene with the highest CO for Thymoquinone in the group and 4, 5, 7,-trihydroxyflavone with the highest CS.

2 Introduction

Bacteriostatic antibiotics limit the growth of bacteria through interaction disruption with (1) bacterial protein production, (2) DNA replication, or (3) other aspects of bacterial cellular metabolism. [1] The following ratios (a) carbon/ oxygen CO, (b) hydrogen/carbon HC, (c) nitrogen/oxygen NO, and (d) carbon/sulfur CS can be used to examine the molecular attributes of chemical compounds for classification. [1] Bacteria based on the structural characteristics of their cell walls where thick layers are Gram-positive for the cell wall while the thin "Gram-negative" are grouped by (a) Gram-positive cocci, (b) Gram-positive bacilli, (c) Gram-negative cocci and (d) Gram-negative bacilli. , the presence of over a thousand bacterial species in the normal human gut flora of the intestines can contribute to (1) gut immunity, (2) synthesise vitamins, i.e. folic acid, vitamin K and biotin, (3) convert sugars to lactic acid like Lactobacillus, as well as (4) fermenting complex undigestible carbohydrates. The presence of this gut flora inhibits the growth of potentially pathogenic bacteria by competitive exclusion and these beneficial bacteria are consequently sold as probiotic dietary supplements. [1]

Pathogens are bacteria that form a parasitic association with other organisms. There are many types of antibiotics and each class inhibits a process different in the pathogen from in the host. Antibiotics produce selective toxicity such as (1) chloramphenicol and (2) puromycin-inhibit the bacterial ribosome not the structurally different eukaryotic ribosome. [1]

Erythromycin is a macrolide antibiotic used to treat and prevent a wide variety of bacterial infections and stops the growth of bacteria. Erythromycin is an inhibitor of the cytochrome P450 system. By binding to the 50s subunit of the bacterial rRNA complex, protein synthesis and subsequent structure and function processes critical for life or replication are inhibited. [1]

Here Table 1 has the different mycins for gene expression interactions with a sample of 30 from 197. Most of erythromycin is metabolised by demethylation in the liver by the hepatic enzyme CYP3A4. Its main elimination route is in the bile with little renal excretion, 2-15 percent unchanged drug. Erythromycin's elimination half-life ranges between 1.5 and 2.0 hours and is between 5 and 6 hours in patients with end-stage renal disease. Erythromycin levels peak in the serum 4 hours after dosing; ethylsuccinate peaks 0.5-2.5 hours after dosing and can be delayed if digested with food [1]

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	NAME	SMILES
3055	puromycin	[Cl-].COc1ccc(C[C@H](N)C(=O)NC2C(CO)OC(C2O)n3cnc4c(ncnc34)N(C)C)cc1
94945	questiomycin a	NC1=CC2=Nc3ccccc3OC2=CC1=O
83340	iyomycin b1	
185	Cactinomycin	C[C@H]1C[C@H](C)C(=O)[C@@H](C1)[C@H](O)CC2CC(=O)NC(=O)C2
93419	steffimycin	COC1C(O)C(O)C(C)OC1OC2C(OC)C(C(O)C(=O)c3cc4C(=O)c5cc(OC)cc(O)c5C(=O)c4c(O)c23
88468	etamycin	CC(C)CC1NC(=O)C(NC(=O)c2ncccc2O)C(C)OC(=O)C(N(C)C(=O)C(C)NC(=O)C(C(C)C(C)C)N(C)C(=O)CN(C)C(=O)C3CC(O)CN3C1=O)c4ccccc4
65381	aquamycin	NC(=O)C#CC(=O)N
26980	Mitomycin	CO[C@]12[C@H]3N[C@H]3CN1C4=C([C@H]2COC(=O)N)C(=O)C(=C(C)C4=O)N
38643	aquamycin	NC(=O)C#CC(=O)N
71935	duramycin	
87222	actinomycin vii	CCC(C)C1NC(=O)C(NC(=O)C2=C(N)C(=O)C(=C3Oc4c(C)ccc(C(=O)NC5C(C)OC(=O)C(C(C)C)N(C)C(=O)CN(C)C(=O)C6CCCN6C(=O)C(NC5=O)C(C)CC)c4N=C23)C)C(C)OC(=O)C(C(C)C)N(C)C(=O)CN(C)C(=O)C7CCCN7C1=O
76411	olivomycin	COC(C1Cc2cc3cc(OC4CC(OC(=O)C)C(OC5CC(O)C(OC)C(C)O5)C(C)O4)cc(O)c3c(O)c2C(=O)C1OC6CC(OC7CC(OC8CC(C(O)C(OC(=O)C(C)C)C(C)O8)C(O)C(C)O7)C(O)C(C)O6)C(=O)C(O)C(C)O
24559	Mithramycin	CO[C@@H]([C@@H]1Cc2cc3cc(OC4CC(OC5CC(O)C(O)C(C)O5)C(O)C(C)O4)c(C)c(O)c3c(O)c2C(=O)[C@H]1OC6CC(OC7CC(OC8CC(C)(O)C(O)C(C)O8)C(O)C(C)O7)C(O)C(C)O6)C(=O)[C@@H](O)[C@@H](C)O
99733	reumycin	CN1C(=O)N=C2NN=CN=C2C1=O
13502	echinomycin	CSC1SCC2N(C)C(=O)C(C)NC(=O)C(COC(=O)C(C(C)C)N(C)C(=O)C1N(C)C(=O)C(C)NC(=O)C(COC(=O)C(C(C)C)N(C)C2=O)NC(=O)c3cnc4ccccc4n3)NC(=O)c5cnc6ccccc6n5
87221	Actinomycin C3	CCC(C)C1NC(=O)C(NC(=O)C2=C(N)C(=O)C(=C3Oc4c(C)ccc(C(=O)NC5C(C)OC(=O)C(C(C)C)N(C)C(=O)CN(C)C(=O)C6CCCN6C(=O)C(NC5=O)C(C)C)c4N=C23)C)C(C)OC(=O)C(C(C)C)N(C)C(=O)CN(C)C(=O)C7CCCN7C1=O
65346	sangivamycin	NC(=O)c1cn(C2OC(CO)C(O)C2O)c3ncnc(N)c13
56410	Porfiromycin	COC12C(COC(=O)N)C3=C(N1CC4C2N4C)C(=O)C(=C(N)C3=O)C
77038	litomycin	CC1OC2CC(=O)OC2C3=C1C(=O)c4c(O)c5c(C6CC(O)C5(O)C(C)O6)c(O)c4C3=O
51001	carbomycin	CO[C@H]1[C@@H](CC(=O)O[C@H](C)C[C@@H]2OC2\C=C\C(=O)[C@H](C)C[C@H](CC=O)[C@@H]1OC3OC(C)C(OC4CC(C)(O)C(OC(=O)CC(C)C)C(C)O4)C(C3O)N(C)C)OC(=O)C
3053	Actinomycin D	CC(C)[C@H]1NC(=O)[C@@H](NC(=O)C2=C(N)C(=O)C(=C3Oc4c(C)ccc(C(=O)N[C@H]5[C@H](C)OC(=O)[C@H](C(C)C)N(C)C(=O)CN(C)C(=O)[C@@H]6CCCN6C(=O)[C@H](NC5=O)C(C)C)c4N=C23)C)[C@H](C)OC(=O)[C@H](C(C)C)N(C)C(=O)CN(C)C(=O)[C@@H]7CCCN7C1=O
82892	nogalamycin compound b	COC(=O)c1c(C)ccc2c(O)c3C(=O)c4c(O)cc5c(OC6(C)OC5(C)C(O)C(C6O)N(C)C)c4C(=O)c3cc12
76627	ossamycin	CC[C@@H](O)C[C@H]1CCC[C@@]2(C[C@@H]3OC(=O)\C=C\[C@@](C)(O)[C@@H](O)[C@H](C)[C@@H](O)[C@H](OC4CCC(C(C)O4)N(C)C)[C@@H](O)[C@](C)(O)CCCCC\C=C\[C@@H]5CC(C)(C)O[C@@]5(O)C[C@H](O2)[C@@H]3C)O1
76455	peliomycin (usan)	
38270	olivomycin	COC(C1Cc2cc3cc(OC4CC(OC(=O)C)C(OC5CC(O)C(OC)C(C)O5)C(C)O4)cc(O)c3c(O)c2C(=O)C1OC6CC(OC7CC(OC8CC(C)(O)C(OC(=O)C(C)C)C(C)O8)C(O)C(C)O7)C(O)C(C)O6)C(=O)C(O)C(C)O
70929	hedamycin	CC1OC(CC(C1O)N(C)C)c2cc(C3CC(C(C(O)C(C)O3)N(C)C)c(O)c4C(=O)c5c6OC(=CC(=O)c6c(C)cc5C(=O)c24)C7(C)OC7C8OC8C
58514	Chromomycin A3	CO[C@@H]([C@@H]1Cc2cc3cc(OC4CC(OC5CC(O)C(OC)C(C)O5)C(OC(=O)C)C(C)O4)c(C)c(O)c3c(O)c2C(=O)[C@H]1OC6CC(OC7CC(OC8CC(C)(O)C(OC(=O)C)C(C)O8)C(O)C(C)O7)C(O)C(C)O6)C(=O)[C@@H](O)[C@@H](C)O
70845	nogalamycin	COC1C(C)OC(O[C@H]2C[C@](C)(O)[C@H](C(=O)OC)c3cc4C(=O)c5c6O[C@H]7O[C@](C)([C@H](O)[C@H]([C@@H]7O)N(C)C)c6cc(O)c5C(=O)c4c(O)c23)C(OC)C1(C)OC
58239	blastmycin	CCCC[C@@H]1[C@@H](OC(=O)CC(C)C)[C@H](C)OC(=O)[C@@H](NC(=O)c2cccc(NC=O)c2O)[C@@H](C)OC1=O
61586	phleomycin (8ci 9ci)	[R]C(=O)c1csc(n1)C2CSC(=N2)CCNC(=O)C(NC(=O)C(C)C(O)C(C)NC(=O)C(NC(=O)c3nc(nc(N)c3C)C(CC(=O)N)NCC(N)C(=O)N)C(OC4OC(CO)C(O)C(O)C4OCCC5OC(CO)C(O)C(OC(=O)N)C5O)c6c[nH]cn6)C(=O)C

Bacteriostatic antibiotics limit the growth of bacteria by interfering with bacterial protein production, DNA replication, or other aspects of bacterial cellular metabolism required to work with the immune system to remove the microorganisms from the body. However, there is not always a precise distinction between them and bactericidal antibiotics; high concentrations of some bacteriostatic agents are also bactericidal, whereas low concentrations of some bactericidal agents are bacteriostatic. [1]

This group includes:

1. Chloramphenicol
2. Clindamycin
3. Ethambutol
4. Lincosamides
5. Macrolides
6. Nitrofurantoin
7. Novobiocin
8. Oxazolidinone
9. Spectinomycin
10. Sulfonamides
11. Tetracyclines
12. Tigecycline
13. Trimethoprim

Consider Novobiocin biosynthesis is related to Arginine and proline metabolism, Phenylalanine, tyrosine and tryptophan biosynthesis and Polyketide sugar unit biosynthesis demonstrated in Figure 1. [1]

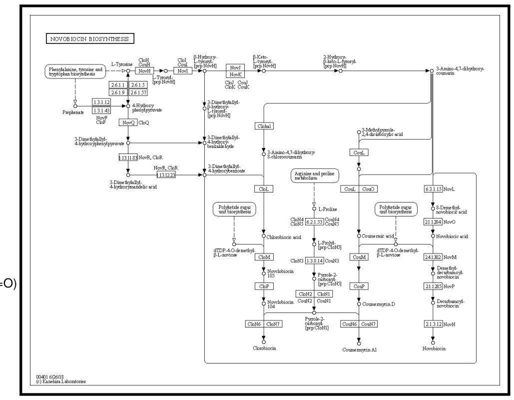

Figure 1: Novobiocin biosynthesis [400]

Coumermycin (USAN); Coumermycin A1 Formula C55H59N5O20 Exact mass 1109.3753 Mol weight 1110.0785 with molecular structure show in both Figure 2 and 3. [1]

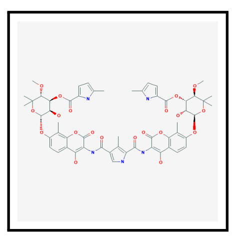

Figure 2: 4434-05-3 500 [400]

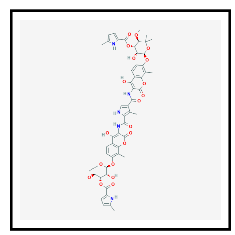

Figure 3: Coumermycin A1 [400]

Based on the similarites of Coumermycin A1 for CO, HC, NO and CS for Table 2.

	CO	HC	NO	CS
1	Min. :2.278	Min. :0.00000	Min. :0.1667	Min. : 0.0000
2	1st Qu.:2.750	1st Qu.:0.07374	1st Qu.:0.2500	1st Qu.: 0.0000
3	Median :2.750	Median :0.10909	Median :0.2500	Median : 0.0000
4	Mean :2.759	Mean :0.09694	Mean :0.2529	Mean : 0.7639
5	3rd Qu.:2.789	3rd Qu.:0.14545	3rd Qu.:0.2632	3rd Qu.: 0.0000
6	Max. :3.353	Max. :0.19512	Max. :0.3500	Max. :55.0000

Consider the following molecular features

1. Molecular weight [MW], [MWT], [MOLWT]
2. Chemical elements [ELMT], [EL]

3. Non-Hydrogen atoms [HAC], [HACNT]
4. Isotope count [IAC], [IACNT]
5. Total formal charge [TFC], [CHG], [CHRG]
6. Chiral atom count [ACC], [ACCNT]
7. Defined chiral atom count [ACDC], [ACDCNT]
8. Undefined chiral atom count [ACUC], [ACUCNT]
9. Hydrogen bond acceptor count [HBAC], [HBACNT]
10. Hydrogen bond donor count [HBDC], [HBDCNT]
11. Tautomer count [TC], [TCNT], [TTMC]
12. Rotatable bond count [RBC], [RBCNT]
13. XLogP[13] [XLGP], [LOGP]

Lipinski's rule states that, in general, an orally active drug has no more than one violation of the following criteria:

1. No more than 5 hydrogen bond donors (the total number of nitrogen–hydrogen and oxygen–hydrogen bonds)
2. No more than 10 hydrogen bond acceptors (all nitrogen or oxygen atoms)
3. A molecular mass less than 500 daltons
4. An octanol-water partition coefficient (log P) that does not exceed 5

Note that all numbers are multiples of five, which is the origin of the rule's name. As with many other rules of thumb, such as Baldwin's rules for ring closure, there are many exceptions. In an attempt to improve the predictions of druglikeness, the rules have spawned many extensions, for example the Ghose filter:

1. Partition coefficient log P in 0.4 to +5.6 range
2. Molar refractivity from 40 to 130
3. Molecular weight from 180 to 480
4. Number of atoms from 20 to 70 (includes H-bond donors [e.g. OHs and NHs] and H-bond acceptors [e.g. Ns and Os])

Veber's Rule further questions a 500 molecular weight cutoff. The polar surface area and the number of rotatable bonds has been found to better discriminate between compounds that are orally active and those that are not for a large data set of compounds in the rat. In particular, compounds which meet only the two criteria of:

1. 10 or fewer rotatable bonds and
2. Polar surface area no greater than 140 Å2

are predicted to have good oral bioavailability.

Here mw, polararea, complexity, xlogp, heavycnt, hbonddonor, hbondacc, and rotbonds with 72 compounds in the sample are provide in Table 3.

	mw	polararea	complexity	xlogp	heavycnt	hbonddonor	hbondac	rotbonds
1	Min. :707.6	Min. :244.0	Min. :1460	Min. :0.300	Min. :51.00	Min. :7.000	Min. :14.00	Min. :8.00
2	1st Qu.:1106.6	1st Qu.:327.0	1st Qu.:2392	1st Qu.:4.600	1st Qu.:79.00	1st Qu.:8.000	1st Qu.:19.00	1st Qu.:16.00
3	Median :1110.1	Median :347.0	Median :2440	Median :4.800	Median :80.00	Median :9.000	Median :20.00	Median :16.00
4	Mean :1126.4	Mean :343.3	Mean :2374	Mean :4.634	Mean :79.81	Mean :8.778	Mean :20.08	Mean :15.86
5	3rd Qu.:1133.1	3rd Qu.:347.0	3rd Qu.:2440	3rd Qu.:5.400	3rd Qu.:80.00	3rd Qu.:9.000	3rd Qu.:20.00	3rd Qu.:16.00
6	Max. :2243.1	Max. :694.0	Max. :3590	Max. :7.900 NA's :11	Max. :161.00	Max. :18.000	Max. :40.00	Max. :32.00
7								

For xlogp, In the context of pharmacokinetics (body-drug relationship), the distribution coefficient has a strong influence on ADME properties of the drug. Hence the hydrophobicity of a compound (distribution coefficient) is a major determinant of how drug-like it is. More specifically, for a drug to be orally absorbed, it normally must first pass through lipid bilayers in the intestinal epithelium (transcellular transport). For efficient transport, the drug must be hydrophobic enough to partition into the lipid bilayer, but not so hydrophobic, that once it is in the bilayer, it will not partition out again. Likewise, hydrophobicity plays a major role in determining where drugs are distributed within the body after absorption and, as a consequence, in how rapidly they are metabolized and excreted. [4]

3 Results

In Drug Resistance, several genes such as CDX2, MUC2, REG4, CDH17, MDR1, SHH, Genomic Instability p53, p21, BAX, p48, GADD45, BAK, POLK and Tumor Progression with Retinoic.Acid, RAR.Beta, RXR are important in the treatment of gastric cancer. Specifically, in Table 4 both MUC2 and MUC5AC are deregulated and overexpression in cancer decreased ERK signaling.

Table 1

Gene	Descriptive
MUC1, MUC4	interact with ERbB mediates HER2 and MAPK, PI3K and C-SRC
MUC1	overexpression with several epithelial and transcriptional regulation with GC rich with Sp1, AP1, AP2 AP3, NF-1, ER and STAT transcription factors.
MUC1	promoter contains 4 STAT binding cis-elements and downstream the interferon signaling pathway. Upregulation of MUC1 promoter with INF-gamma and the STAT-1 and STAT-3 activation by IL-6
MUC1	expression upregulates HIF-1
MUC5A	C overexpression airway inflammation conditions
MUC4	mediated by PI3K/AKT, ERK1/2 and SRC/FAK
CA125/MUC16	modulates EGFR interacts with ERM domain
MUC2 and MUC5AC	deregulated and overexpression in cancer decreased ERK signaling
MUC2	overexpression 5-FU (fluorouracil) and methotrexate (chemo postive relationship with MUC2)
MUC4	resistence to chemo agents and down regulation of chemosensitization
MUC1	overexpression
MUC1	or MUC4 silencing to the drug trastuzumab

Table 5 has the list of compounds used in the treatment of deregulated and overexpression of both MUC2 and MUC5AC.

	Chem.Smiles
1	C1=CC(=C(C=C1C2=C(C(=O)C3=C(C=C(C=C3O2)O)O)O)O)O
2	C1=CC(=CC=C1C2=C(C(=O)C3=C(O2)C=C(C(=C3O)C4C(C(C(C(O4)CO)O)O)O)O)C5C(C(C(C(O5)CO)O)O)O)O
3	C1=CC(=CC=C1C2=CC(=O)C3=C(C(=C(C=C3O2)OC4C(C(C(C(O4)C(=O)O)O)O)O)O)O)O
4	C1C(C(OC2=CC(=CC(=C21)O)O)C3=CC(=C(C=C3)O)O)OC(=O)C4=CC(=C(C(=C4)O)O)O
5	CC=C1C(=O)CC2C1(CCC3C2CCC4=CC(=O)CCC34C)C
6	CC1=CC(=O)C(=CC1=O)C(C)C
7	CC1CCC2(CCC3(C(=CCC4C3(CCC5C4(CCC(C5(C)C)O)O)C)C)C2C1C)C)C(=O)O
8	COC1=C(C=CC(=C1)C2C(OC3=C(O2)C=C(C=C3)C4C(C(=O)C5=C(C=C(C=C5O4)O)O)O)CO)O

Figure 4 has the element spatial arrangements and bond patterns for the eight compounds.

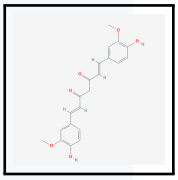

Figure 4: Curcumin [602]

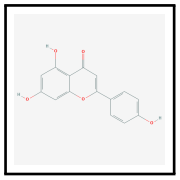

Figure 5: Apigenin [602]

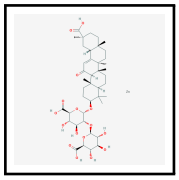

Figure 6: Licorice [602]

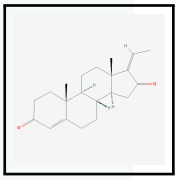

Figure 7: Guggulsterone [602]

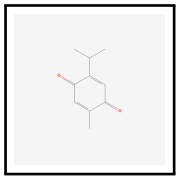

Figure 8: Thymoquinone [602]

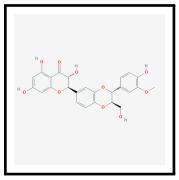

Figure 9: Silibinin [602]

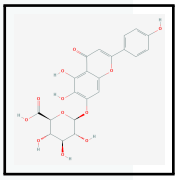

Figure 10: Scutellarin [602]

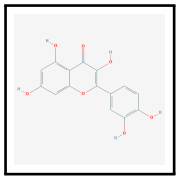

Figure 11: Quercetin [602]

Figure 12: Ursolic acid [602]

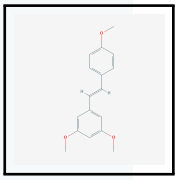

Figure 13: (E)-3,5,4'-Trimethoxystilbene [602]

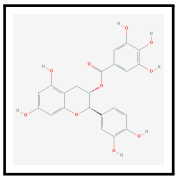

Figure 14: (+)-Epicatechin-3-O-gallate [602]

3.1. Compound 1:diferuloylmethane

Table 6 has the ratio of CO, HC, NC and CS for the compound diferuloylmethane.

	CO	HC	NO	CS
1	Min. :0.6522	Min. :0.00000	Min. :0.000000	Min. : 0.0000
2	1st Qu.:2.2500	1st Qu.:0.00000	1st Qu.:0.000000	1st Qu.: 0.0000
3	Median :2.6667	Median :0.00000	Median :0.000000	Median : 0.0000
4	Mean :2.7923	Mean :0.01137	Mean :0.002214	Mean : 0.4975
5	3rd Qu.:3.2000	3rd Qu.:0.00000	3rd Qu.:0.000000	3rd Qu.: 0.0000
6	Max. :7.8571	Max. :0.40000	Max. :0.600000	Max. :30.0000

3.2. Compound 2:4, 5, 7,-trihydroxyflavone

Table 7 has the ratio of CO, HC, NC and CS for the compound 2:4, 5, 7,-trihydroxyflavone.

	CO	HC	NO	CS
1	Min. :1.350	Min. :0.0000	Min. :0.000000	Min. : 0.0000
2	1st Qu.:1.929	1st Qu.:0.0000	1st Qu.:0.000000	1st Qu.: 0.0000
3	Median :2.333	Median :0.1000	Median :0.000000	Median : 0.0000
4	Mean :2.748	Mean :0.1380	Mean :0.000263	Mean : 0.9054
5	3rd Qu.:3.333	3rd Qu.:0.2381	3rd Qu.:0.000000	3rd Qu.: 0.0000
6	Max. :8.750	Max. :0.6522	Max. :0.272727	Max. :28.0000

3.3. Compound 3: Glycyrrhiza glabra

Table 8 has the ratio of CO, HC, NC and CS for the compound Glycyrrhiza glabra.

	CO	HC	NO	CS
1	Min. :0.7941	Min. :0.0000	Min. :0.0000000	Min. : 0.0000
2	1st Qu.:1.6923	1st Qu.:0.0000	1st Qu.:0.0000000	1st Qu.: 0.0000
3	Median :1.8333	Median :0.1905	Median :0.0000000	Median : 0.0000
4	Mean :1.9168	Mean :0.1768	Mean :0.0002596	Mean : 0.2288
5	3rd Qu.:2.0667	3rd Qu.:0.2727	3rd Qu.:0.0000000	3rd Qu.: 0.0000
6	Max. :8.6364	Max. :0.6667	Max. :0.1428571	Max. :34.0000

3.4. Compound 4: guggulsterone

Table 9 has the ratio of CO, HC, NC and CS for the compound guggulsterone.

	CO	HC	NO	CS
1	Min. :0.6286	Min. :0.00000	Min. :0.0000000	Min. : 0.0000
2	1st Qu.:2.0952	1st Qu.:0.00000	1st Qu.:0.0000000	1st Qu.: 0.0000
3	Median :2.4444	Median :0.05263	Median :0.0000000	Median : 0.0000
4	Mean :2.6181	Mean :0.06754	Mean :0.0003857	Mean : 0.2024
5	3rd Qu.:3.0000	3rd Qu.:0.10714	3rd Qu.:0.0000000	3rd Qu.: 0.0000
6	Max. :9.3000	Max. :0.37037	Max. :0.2000000	Max. :30.0000

3.5. Compound 5: Thymoquinone

Table 10 has the ratio of CO, HC, NC and CS for the compound Thymoquinone.

	CO	HC	NO	CS
1	Min. : 3.167	Min. :0.00000	Min. :0.0000000	Min. : 0.0000
2	1st Qu.:10.000	1st Qu.:0.05263	1st Qu.:0.0000000	1st Qu.: 0.0000
3	Median :11.500	Median :0.15000	Median :0.0000000	Median : 0.0000
4	Mean :15.377	Mean :0.13144	Mean :0.0003447	Mean : 0.2273
5	3rd Qu.:21.000	3rd Qu.:0.19048	3rd Qu.:0.0000000	3rd Qu.: 0.0000
6	Max. :42.000	Max. :0.63158	Max. :0.5000000	Max. :33.0000

3.6. Compound 6: Silibinin

Table 11 has the ratio of CO, HC, NC and CS for the compound Thymoquinone.

	CO	HC	NO	CS
1	Min. : 3.000	Min. :0.00000	Min. :0.000000	Min. :0
2	1st Qu.: 5.500	1st Qu.:0.00000	1st Qu.:0.000000	1st Qu.:0
3	Median : 7.333	Median :0.00000	Median :0.000000	Median :0
4	Mean : 7.547	Mean :0.01129	Mean :0.002762	Mean :0
5	3rd Qu.:10.000	3rd Qu.:0.00000	3rd Qu.:0.000000	3rd Qu.:0
6	Max. :14.000	Max. :1.11111	Max. :0.500000	Max. :0

3.7. Compound 7: Scutellarin

Table 12 has the ratio of CO, HC, NC and CS for the compound Scutellarin

	CO	HC	NO	CS
1	Min. : 2.727	Min. :0.00000	Min. :0.000000	Min. : 0.0000
2	1st Qu.: 6.200	1st Qu.:0.06667	1st Qu.:0.000000	1st Qu.: 0.0000
3	Median : 7.500	Median :0.12903	Median :0.000000	Median : 0.0000
4	Mean : 8.365	Mean :0.11660	Mean :0.002397	Mean : 0.2718
5	3rd Qu.:10.000	3rd Qu.:0.16667	3rd Qu.:0.000000	3rd Qu.: 0.0000
6	Max. :32.000	Max. :0.30000	Max. :1.000000	Max. :36.0000

3.8. Compound 8: Quercetin, Ursolic acid, 3, 5, 4 -trihydroxy-trans-stilbene

Table 13 has the ratio of CO, HC, NC and CS for the compound Quercetin, Ursolic acid, 3, 5, 4 -trihydroxy-trans-stilbene.

	CO	HC	NO	CS
1	Min. :1.136	Min. :0.00000	Min. :0.0000000	Min. : 0.0000
2	1st Qu.:1.800	1st Qu.:0.00000	1st Qu.:0.0000000	1st Qu.: 0.0000
3	Median :2.111	Median :0.09091	Median :0.0000000	Median : 0.0000
4	Mean :2.377	Mean :0.13008	Mean :0.0005422	Mean : 0.2579
5	3rd Qu.:2.750	3rd Qu.:0.22727	3rd Qu.:0.0000000	3rd Qu.: 0.0000
6	Max. :8.636	Max. :0.66667	Max. :0.5000000	Max. :52.0000

For these 8 compounds. the avg values are shown in Table 14 for comparision.

	CO	HC	NO	CS
1	2.7923	0.01137	0.002214	0.4975
2	2.748	0.1380	0.000263	0.9054
3	1.9168	0.1768	0.0002596	0.2288
4	2.6181	0.06754	0.0003857	0.2024
5	15.377	0.13144	0.0003447	0.2273
6	7.547	0.01129	0.002762	0
7	8.365	0.11660	0.002397	0.2718
8	2.377	0.13008	0.0005422	0.2579

4 Conclusion

In this article, element ratios were examined with respect to Bacteriostatic antibiotics limit the growth of bacteria by interfering with bacterial protein production, DNA replication, or other aspects of bacterial cellular metabolism. They must work together with the immune system to remove the microorganisms from the body. However, there is not always a precise distinction between them and bactericidal antibiotics; high concentrations of some bacteriostatic agents are also bactericidal, whereas low concentrations of some bactericidal agents are bacteriostatic. For (1) diferuloylmethane, (2) 4, 5, 7,-trihydroxyflavone, (3) Glycyrrhiza glabra, (4) guggulsterone, (5) Thymoquinone, (6) Silibinin, (7) Scutellarin and (8) Quercetin, Ursolic acid, 3, 5, 4 -trihydroxy-trans-stilbene with the highest CO for Thymoquinone in the group and 4, 5, 7,-trihydroxyflavone with the highest CS.

5 References

[1] Wikipedia contributors. "Bacteria." Wikipedia, The Free Encyclopedia. Wikipedia, The Free Encyclopedia, 5 Mar. 2021. Web. 6 Mar. 2021.

[2] Wikipedia contributors. "Erythromycin." Wikipedia, The Free Encyclopedia. Wikipedia, The Free Encyclopedia, 29 Dec. 2020. Web. 6 Mar. 2021.

[3] Wikipedia contributors. "Pearson distribution." Wikipedia, The Free Encyclopedia. Wikipedia, The Free Encyclopedia, 12 Feb. 2021. Web. 23 Feb. 2021.

[4] Wikipedia contributors. "Partition coefficient." Wikipedia, The Free Encyclopedia. Wikipedia, The Free Encyclopedia, 4 Mar. 2021. Web. 7 Mar. 2021.

[400] Kanehisa, Furumichi, M., Tanabe, M., Sato, Y., and Morishima, K.; KEGG: new perspectives on genomes, pathways, diseases and drugs. Nucleic Acids Res. 45, D353-D361 (2017).

[401] Kanehisa, M., Sato, Y., Kawashima, M., Furumichi, M., and Tanabe, M.; KEGG as a reference resource for gene and protein annotation. Nucleic Acids Res. 44, D457-D462 (2016).

[402] Kanehisa, M. and Goto, S.; KEGG: Kyoto Encyclopedia of Genes and Genomes. Nucleic Acids Res. 28, 27-30 (2000).

[420] GeneCards Version 3: the human gene integrator

[430] DrugBank 5.0: a major update to the DrugBank database for 2018.

[440] COSMIC: the Catalogue Of Somatic Mutations In Cancer.

[450] Online Mendelian Inheritance in Man (OMIM), a knowledgebase of human genes and genetic disorders

[460] The ClinicalTrials.gov Results Database — Update and Key Issues

[470] PubChem Substance and Compound databases

[480] The STRING database in 2017: quality-controlled protein–protein association networks, made broadly accessible

[490] MalaCards: an amalgamated human disease compendium with diverse clinical and genetic annotation and structured search

[601] Szklarczyk D, Gable AL, Lyon D, et al. STRING v11: protein-protein association networks with increased coverage, supporting functional discovery in genome-wide experimental datasets. Nucleic Acids Res. 2019;47(D1):D607-D613. doi:10.1093/nar/gky1131

[602] Ashburner et al. Gene ontology: tool for the unification of biology. Nat Genet. May 2000;25(1):25-9.

[603] The Gene Ontology Consortium. The Gene Ontology Resource: 20 years and still GOing strong. Nucleic Acids Res. Jan 2019;47(D1):D330-D338

[700] Online SMILES Translator and Structure File Generator

[701] https://www.molport.com/shop/find-chemicals-by-smiles

[800] CAS Common Chemistry - run by the American Chemical Society

[801] Comparative Toxicogenomics Database - run by North Carolina State University

[802] ChEMBL - run by European Bioinformatics Institute

[803] ChemSpider - run by UK's Royal Society of Chemistry

[804] DrugBank - run by the University of Alberta

[805] IUPAC - run by Swiss-based International Union of Pure and Applied Chemistry (IUPAC)

[806] Moltable - run by India's National Chemical Laboratory

[807] PubChem - run by the National Institute of Health, USA

[808] BindingDB - run by the University of California, San Diego

[809] SCRIPDB - run by the University of Toronto, Canada

[810] National Center for Biotechnology Information (NCBI) - run by the National Institute of Health, USA

[811] Entrez - run by the National Institute of Health, USA

[812] GenBank - run by the National Institute of Health, USA

[1000] R Core Team (2015). R: A language and environment for statistical computing. R Foundation for Statistical Computing, Vienna, Austria. URL https://www.R-project.org/.

[1001] Osorio, D., Rondon-Villarreal, P. and Torres, R. Peptides: A package for data mining of antimicrobial peptides. The R Journal. 7(1), 4-14 (2015)