SCIENCE BASED USES OF PLANT EXTRACTS TO IMPROVE ANIMAL HEALTH IN POST ANTIBIOTIC ERA: WHERE ARE WE?

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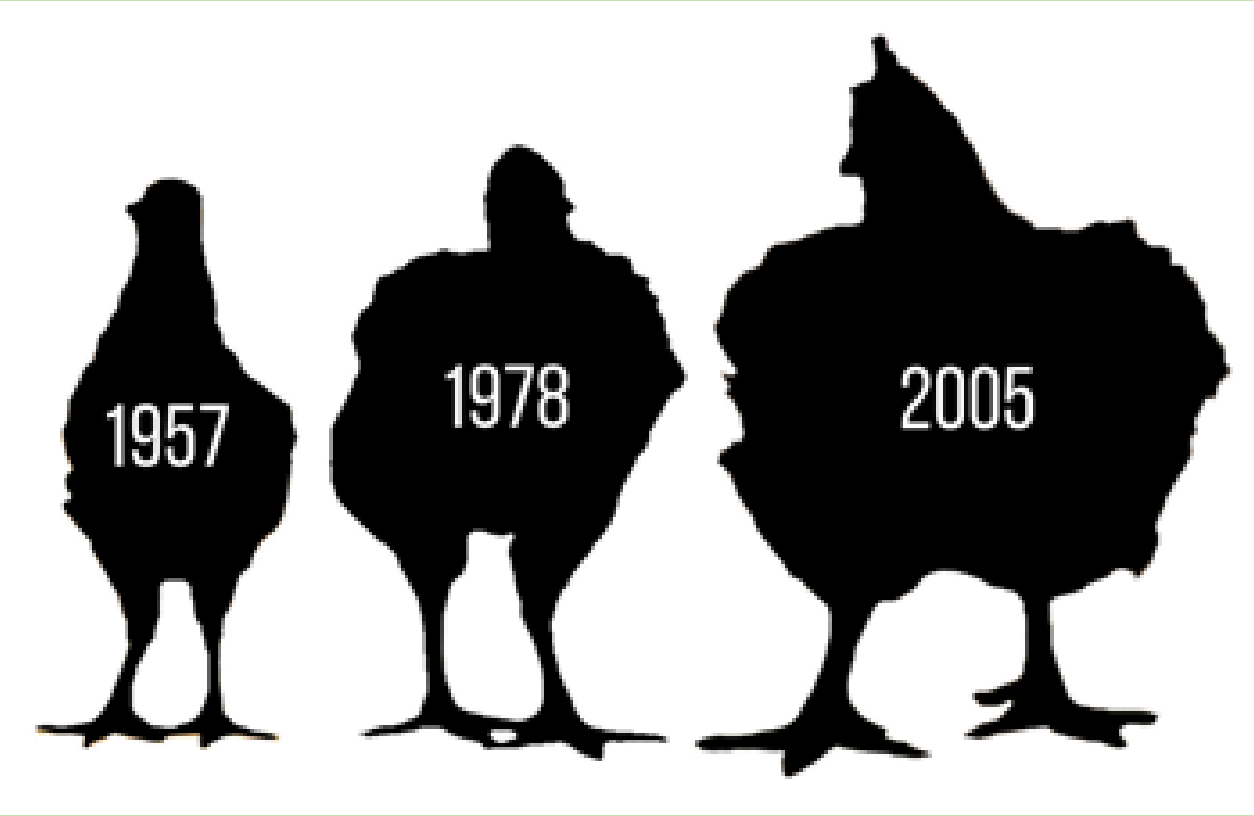
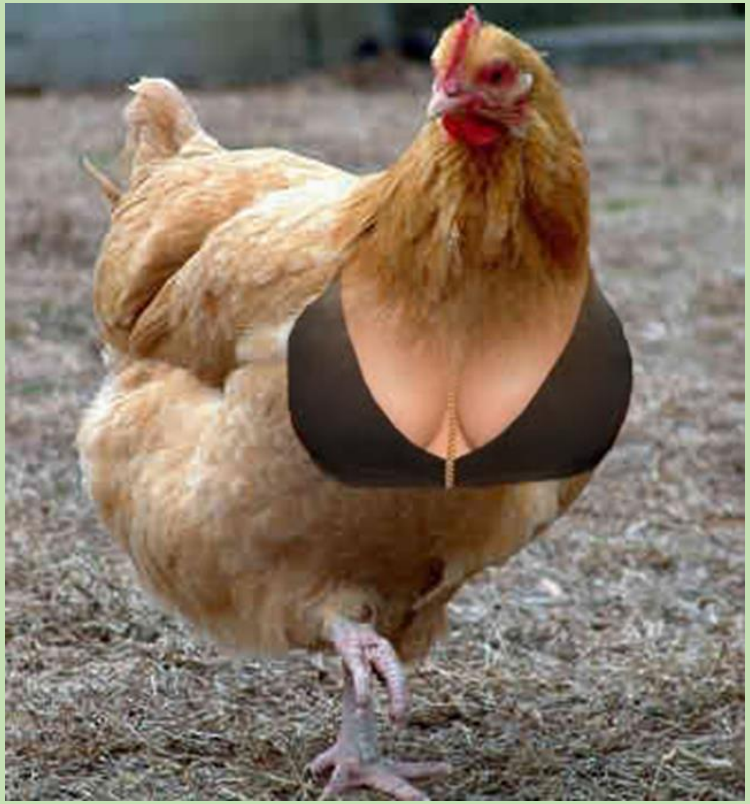
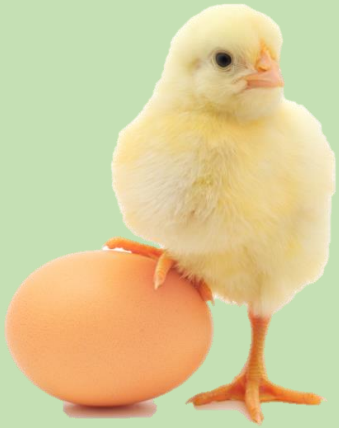
PERFORMANCE HAS INCREASED CONSIDERABLY





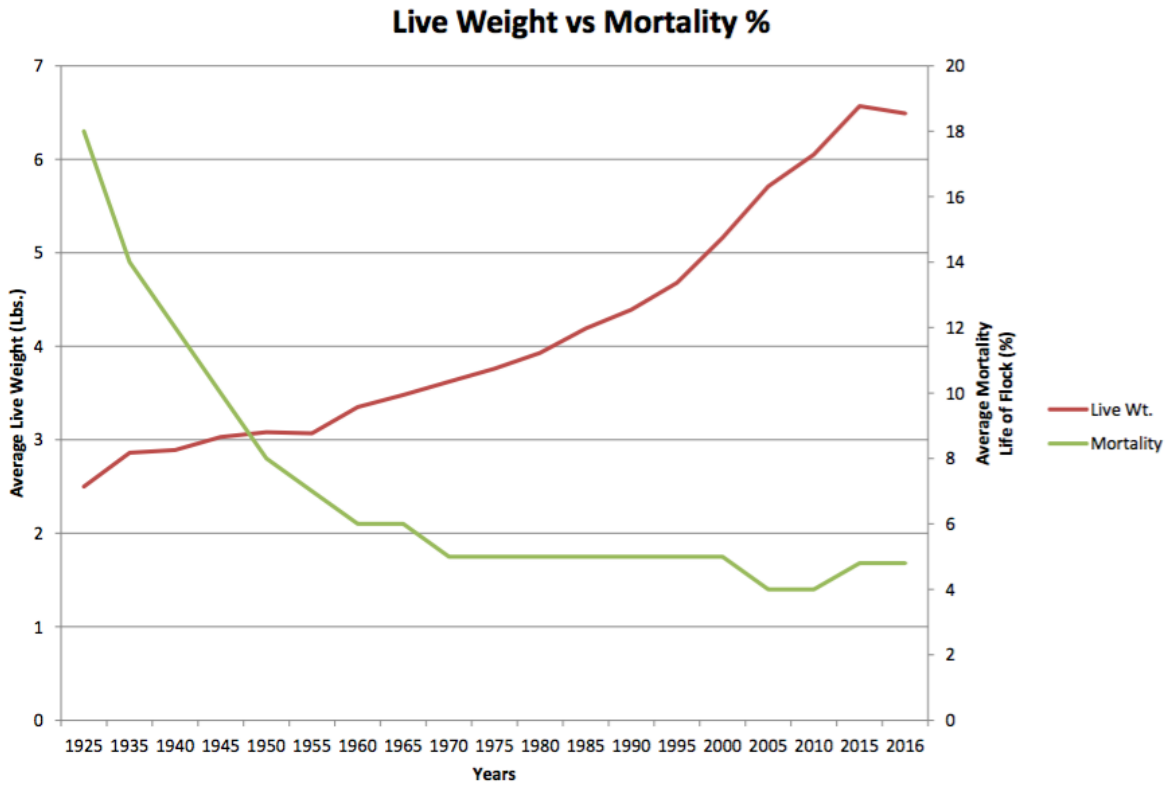
IS THIS TENDENCY ONLY IN BROILERS?

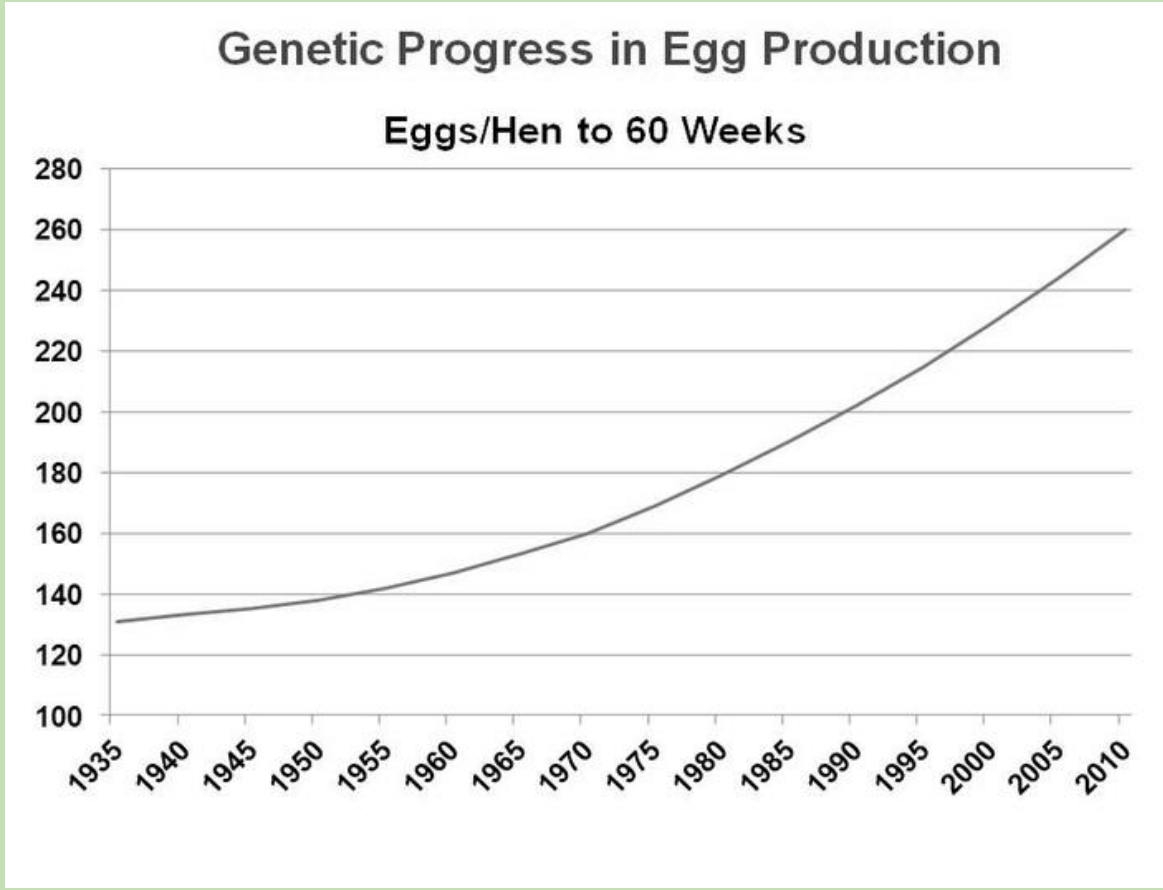


BROIERS	LAYERS	BREEDERS
FCR: 1.6 FOR 2Kg BW	320 EGGS	145-150 CHICKS
MORTALITY 5%		

PRESENT TREND SHOWS A PHENOMENOL PROGRESS IN POULTRY INDUSTRY

Live Weight vs Mortality – Over the last 25 years, the mortality rate of birds on the farm has declined, even as the birds have gotten bigger. If birds were not healthy and thriving, mortality rates would have increased.





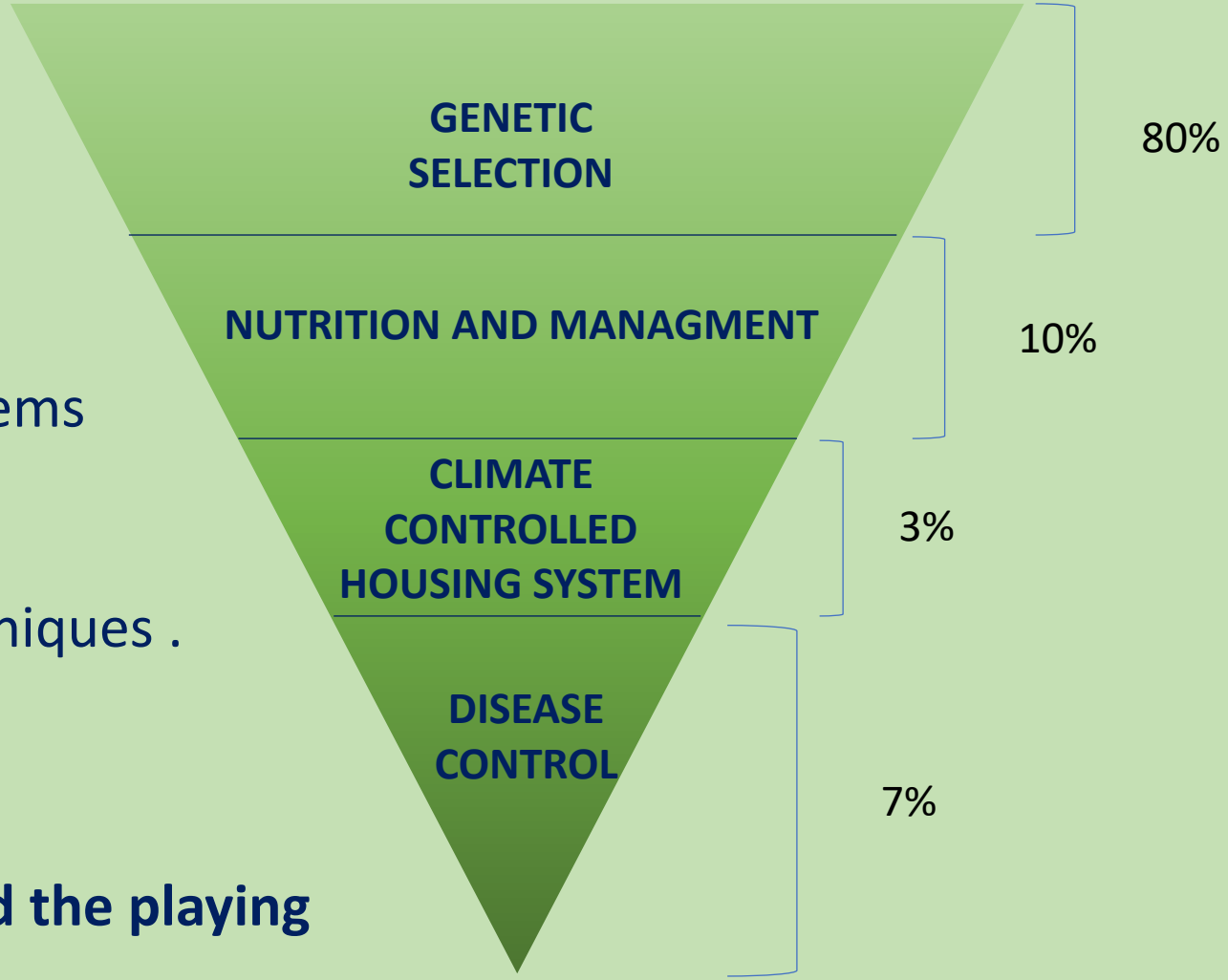
WHAT HAS CONTRIBUTED TO THIS PHENOMENAL PROGRESS IN POULTRY PRODUCTION?

1. Genetic Selection

2. Advances in Nutrition and Management

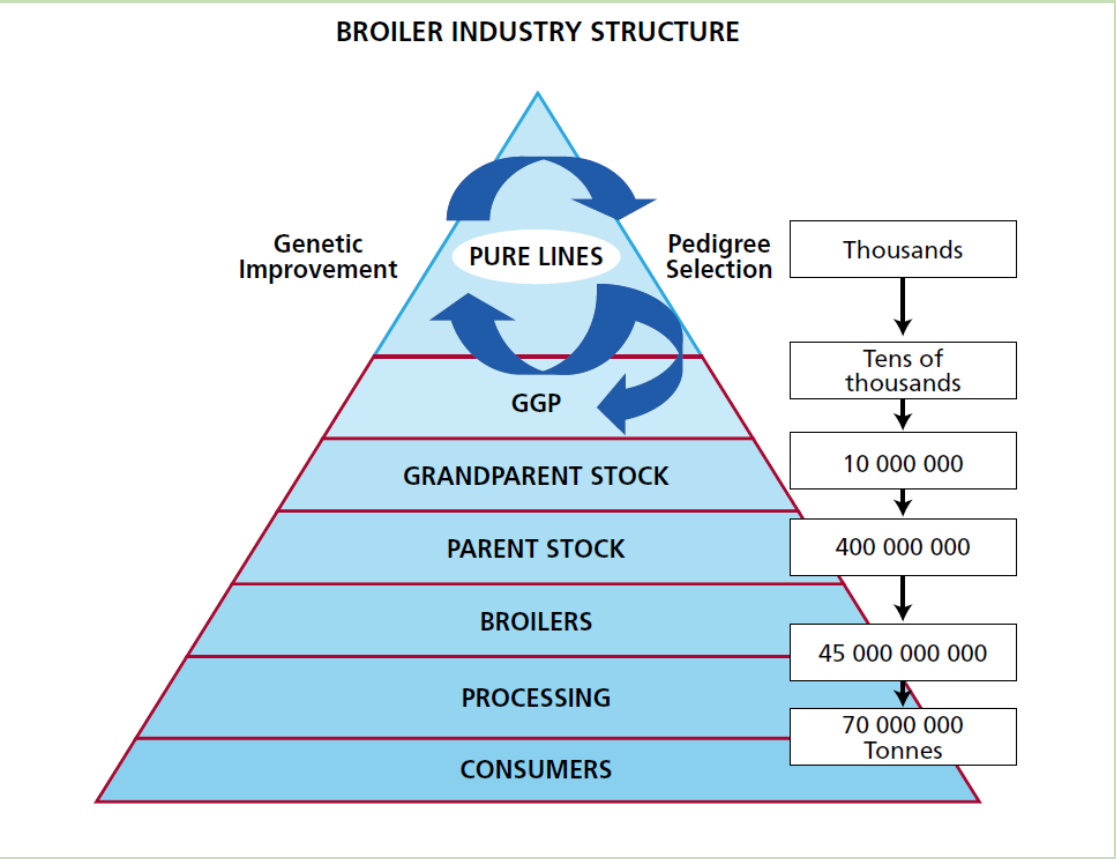
3. Advanced climate controlled housing systems

4. Excellent Disease control
   - Improved Vaccines and vaccination techniques .
   - Effective use of Antibiotics and AGP”S



Obviously, genetic selection has changed the playing field of poultry nutrition.

WHAT HAS CONTRIBUTED TO THIS PHENOMENAL PROGRESS IN POULTRY PRODUCTION?



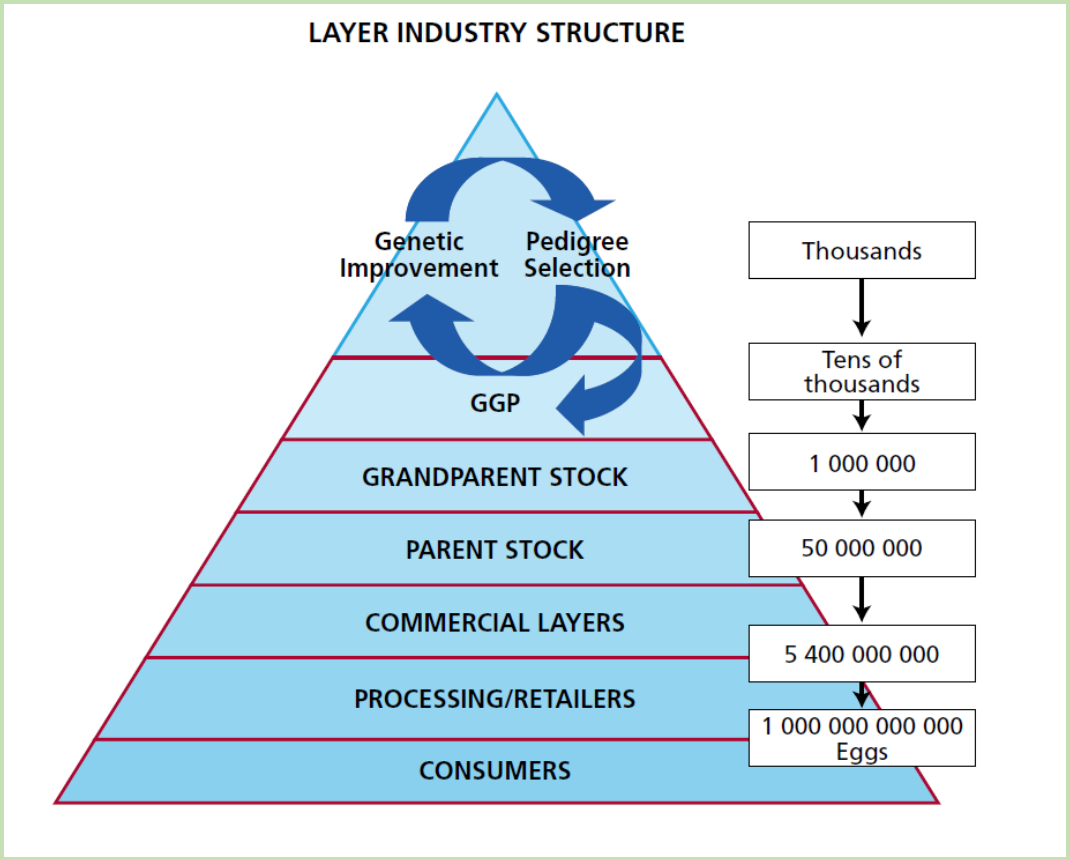
Genetic Selection For-

Feed utilization efficiency

Breast meat yield

Ascites

Skeletal abnormalities



Genetic Selection For-

Egg Production and Size

Egg Quality

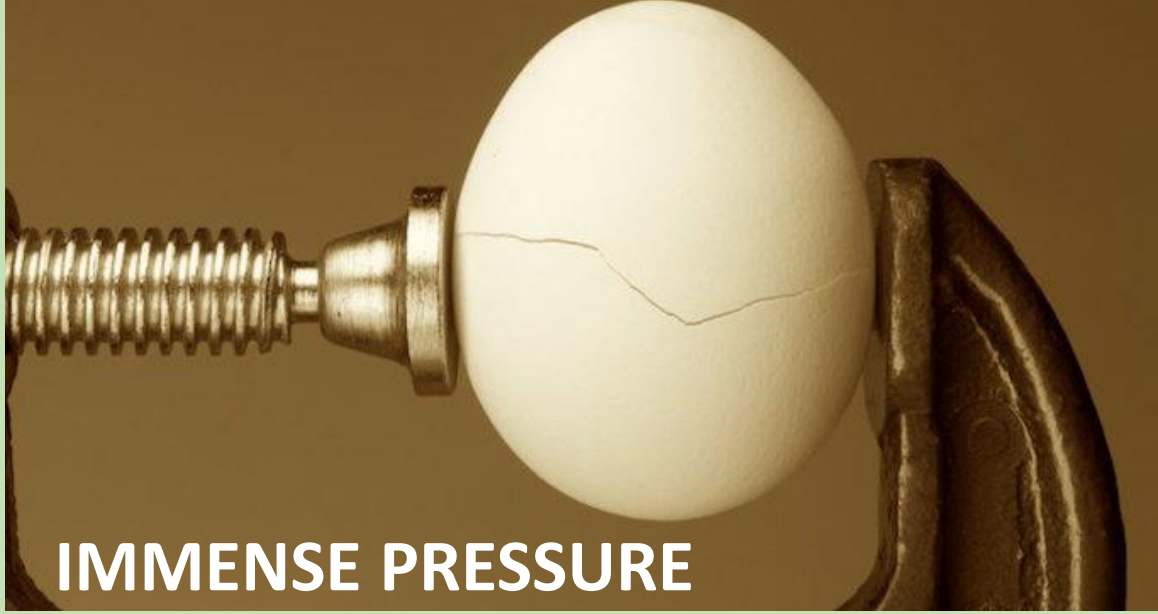
Selection in barn and free range environment

Genetic Selection and Productivity

Have nutritional advances kept pace with genetic potential for growth, and will it continue in the future?

AT PRESENT

Immense pressure on Poultry Industry because of

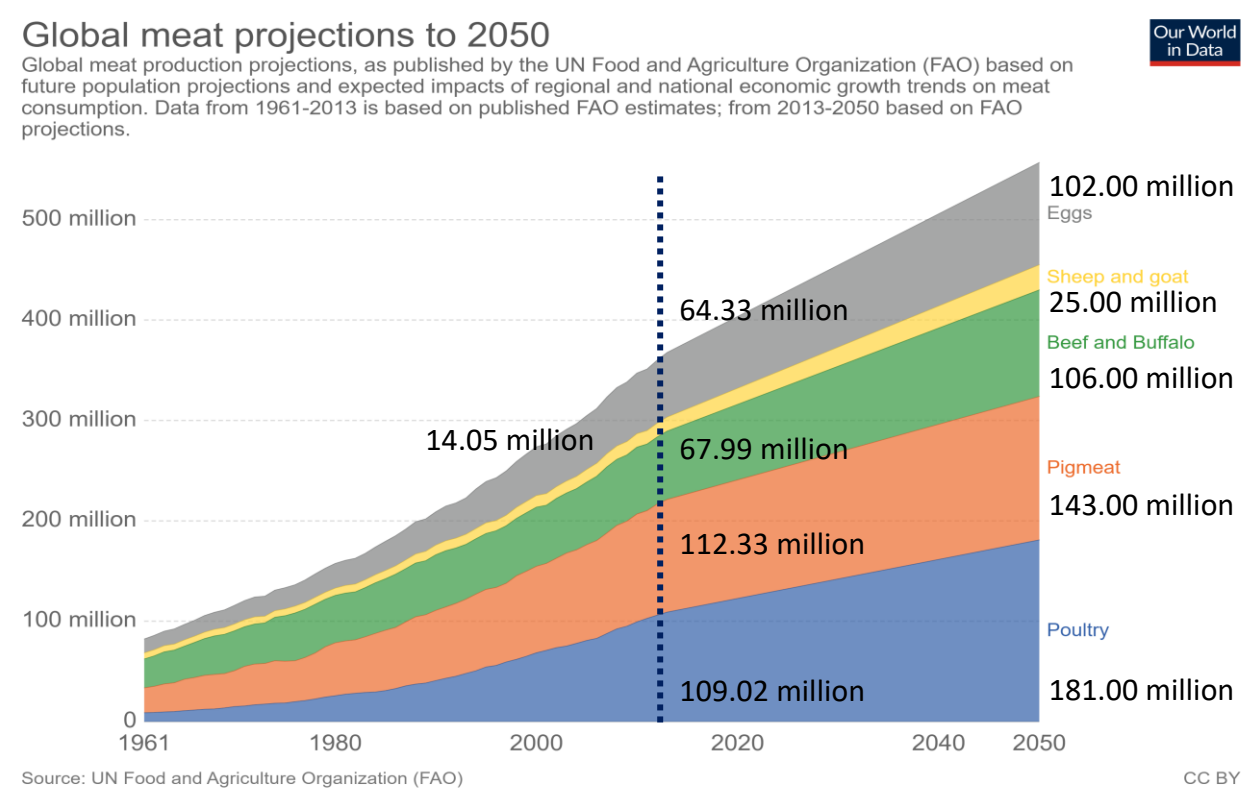


1. High meat demand

2. Frequent challenges & Diseases in the birds

3. Growing Antibiotic Resistance

High Global Meat Demand



Challenges In Animal Protein Production

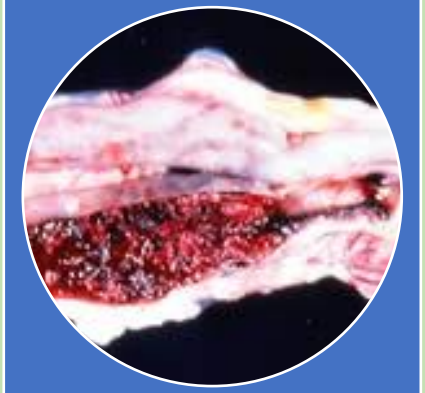
- NEW LEGISLATIONS
- FEED INGREDIENT SUPPLY
- CONSUMER AWARENESS
- SUSTAINABLE PRODUCTION
- MAINTAIN PROFITABILITY

Frequent challenges & Disease in the birds

AVIAR INFLUENZA AND NEW CASTLE DISEASE

INFECTIOUS BRONCHITIS

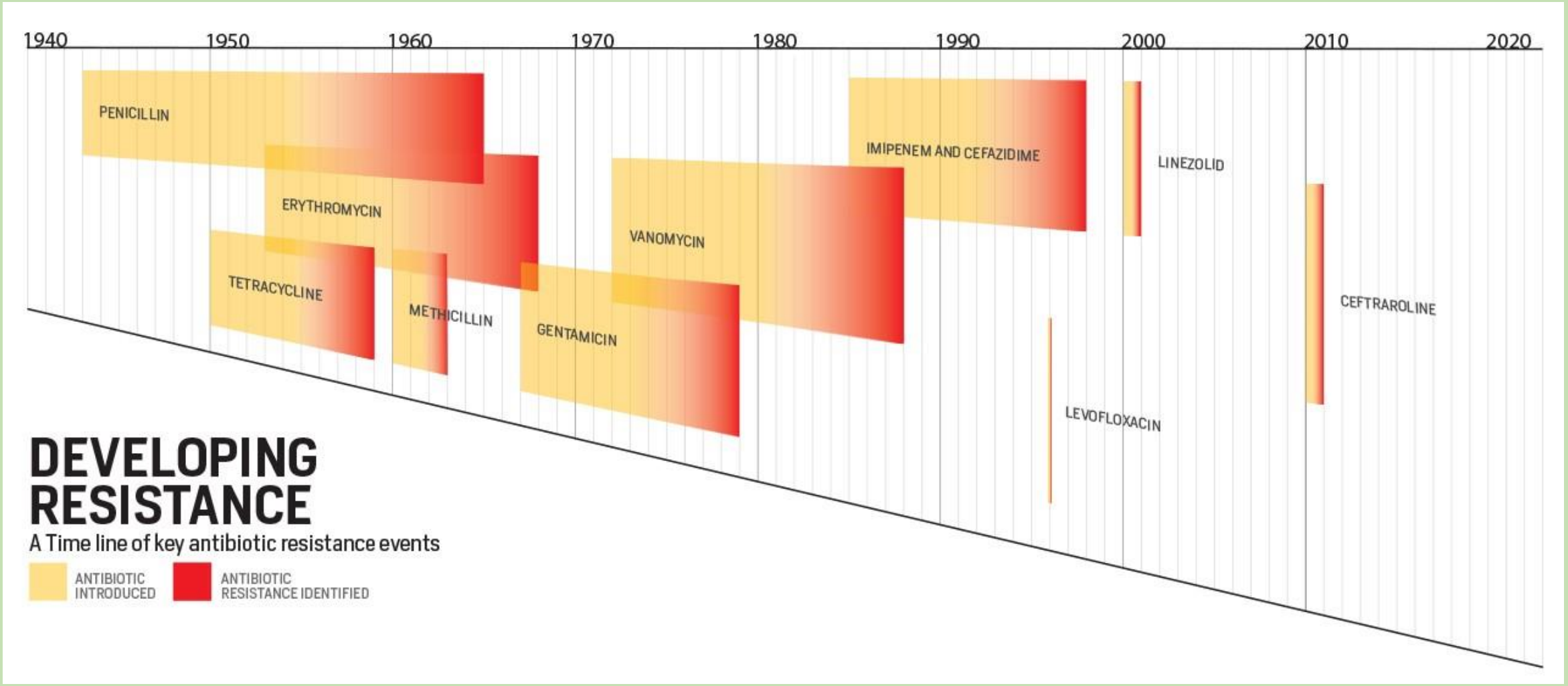
NECROTIC ENTERITIS



COCCIDIOSIS

IMMUNITY OF THE ORGANISM

Antibiotic Resistance



GLOBAL TRENDS IN AB CONSUMPTION

PNAS

Global trends in antimicrobial use in food animals

Thomas P. Van Boeckel[a,1], Charles Brower[b], Marius Gilbert[c,d], Bryan T. Grenfell[a,e,f], Simon A. Levin[a,g,h,1], Timothy P. Robinson[i], Aude Teillant[a,e], and Ramanan Laxminarayan[b,e,j,1]

[a]Department of Ecology and Evolutionary Biology, Princeton University, Princeton, NJ 08544; [b]Center for Disease Dynamics, Economics & Policy, Washington, DC 20036; [c]Universite Libre de Bruxelles, B1050 Brussels, Belgium; [d]Fonds National de la Recherche Scientifique, B1000 Brussels, Belgium; [e]Princeton Environmental Institute, Princeton, NJ 08544; [f]Fogarty International Center, National Institutes of Health, Bethesda, MD 20892; [g]Beijer Institute of Ecological Economics, 10405 Stockholm, Sweden; [h]Resources for the Future, Washington, DC 20036; [i]International Livestock Research Institute, 00100 Nairobi, Kenya; and [j]Public Health Foundation of India, New Delhi 110070, India

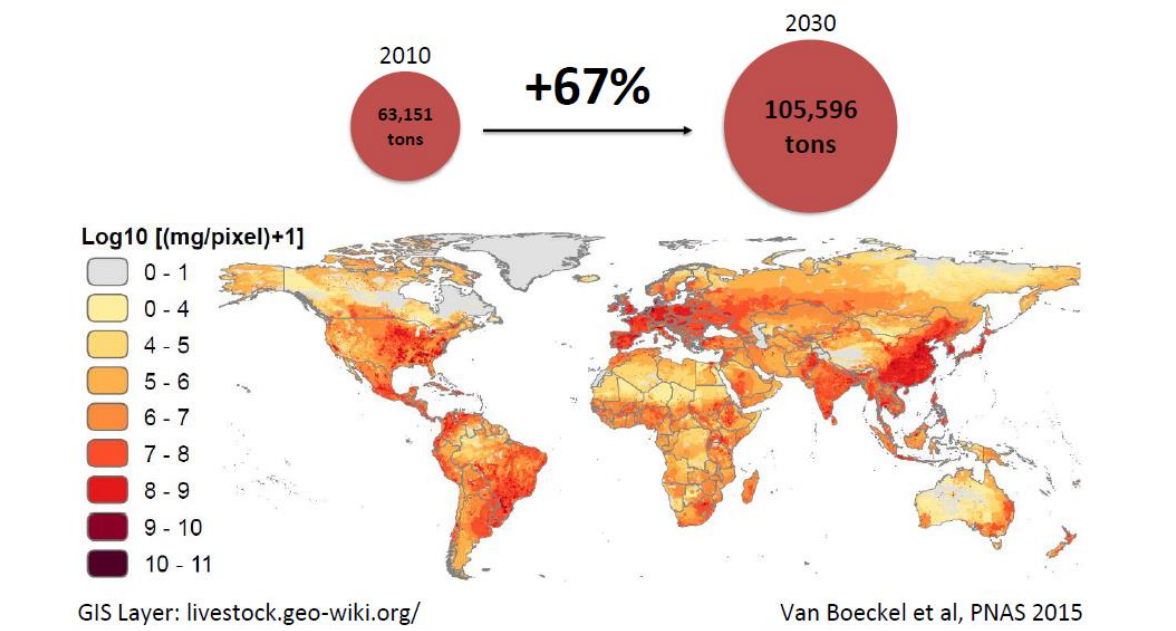
Contributed by Simon A. Levin, February 18, 2015 (sent for review November 21, 2014; reviewed by Delia Grace and Lance B. Price)

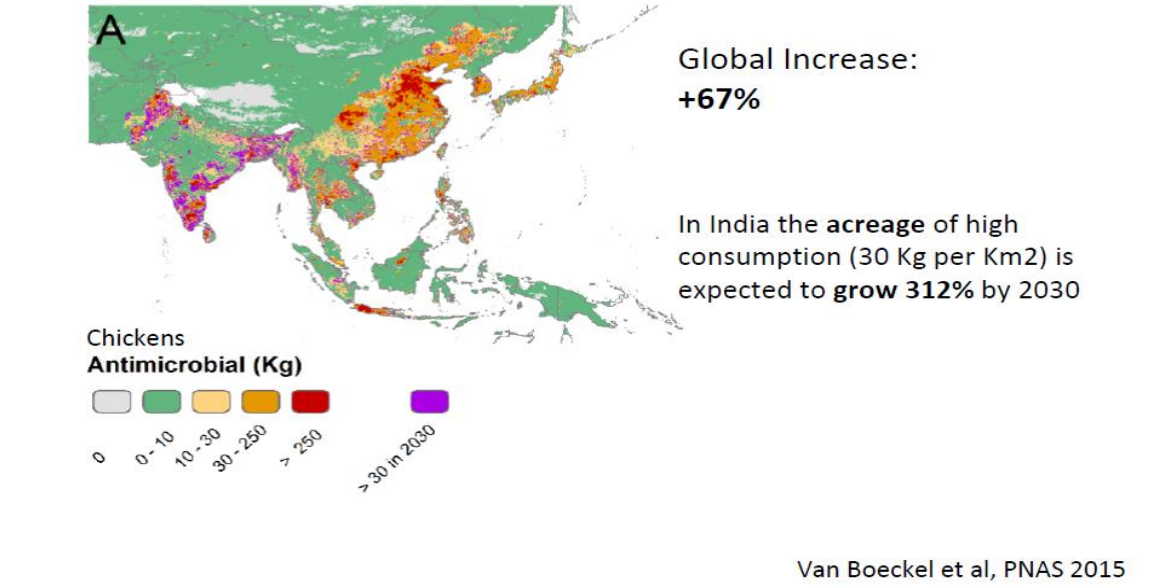
Objectives

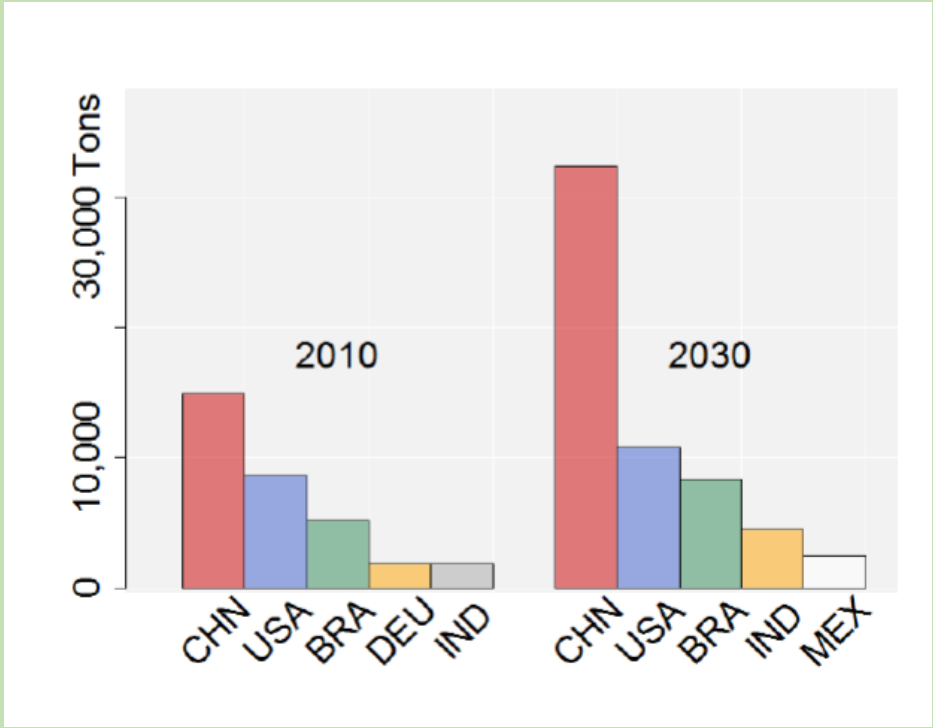
1. **Estimate and map the current consumption(2010) of antimicrobials**

2. **Project the trends for future consumption (2030), if the actions are not taken**

GLOBAL Antimicrobial Consumption In Livestock







Economic Impact- Global Level

THE LANCET Infectious Diseases

Emergence of plasmid-mediated colistin resistance mechanism MCR-1 in animals and human beings in China: a microbiological and molecular biological study

Vol 16 February 2016

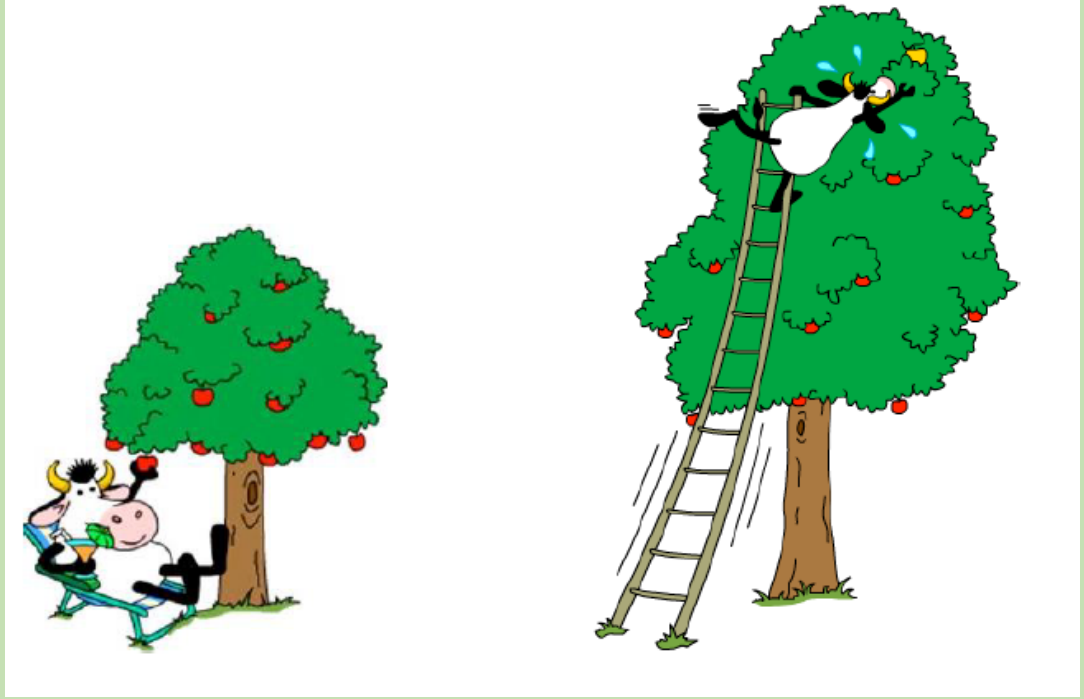
Yi-Yun Liu, Yang Wang*, Timothy R Walsh, Ling-Xian Yi, Rong Zhang, James Spencer, Yohei Doi, Guobao Tian, Baolei Dong, Xianhui Huang, Lin-Feng Yu, Danxia Gu, Hongwei Ren, Xiaojie Chen, Luchao Lv, Dandan He, Hongwei Zhou, Zisen Liang, Jian-Hua Liu, Jianzhong Shen*

www.eurosurveillance.org

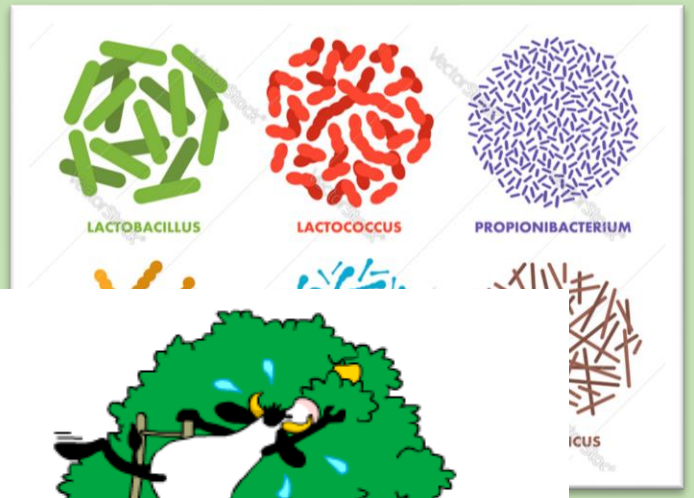
Identification of a novel plasmid-mediated colistin-resistance gene, *mcr-2*, in *Escherichia coli*, Belgium, June 2016

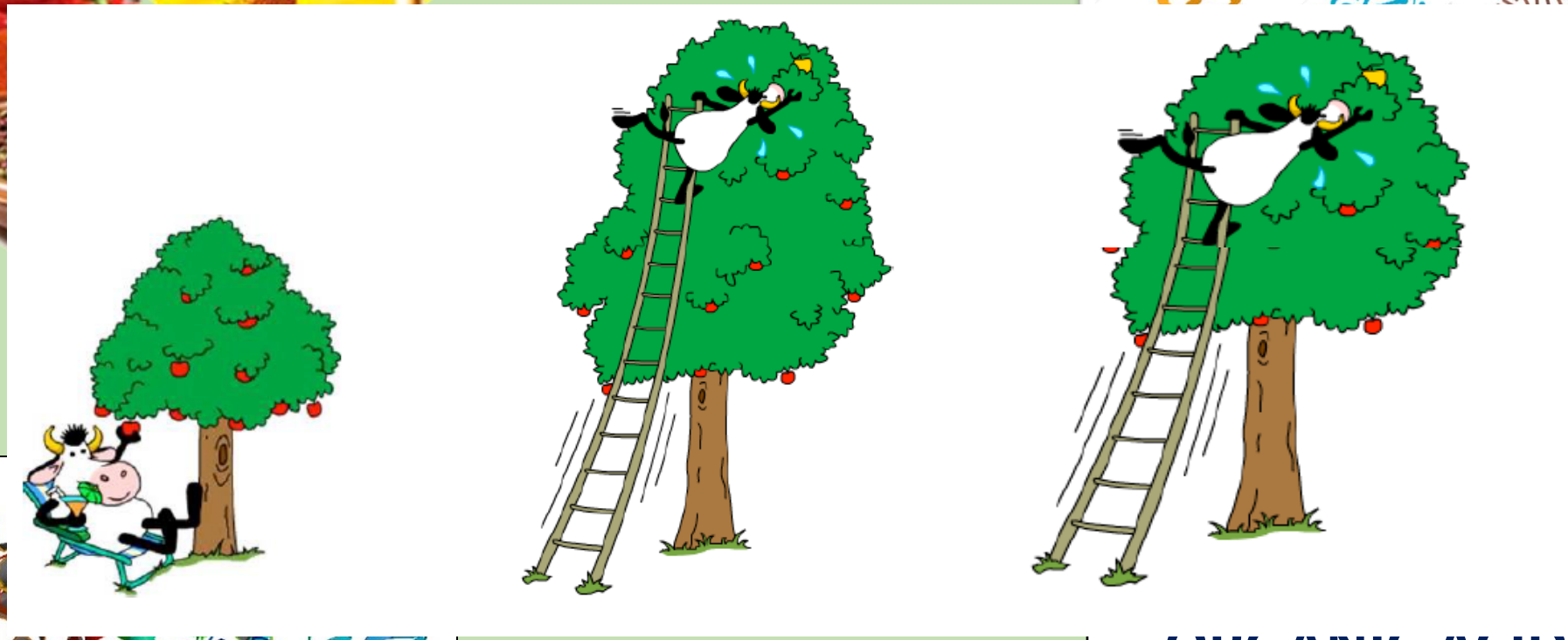
June 2016

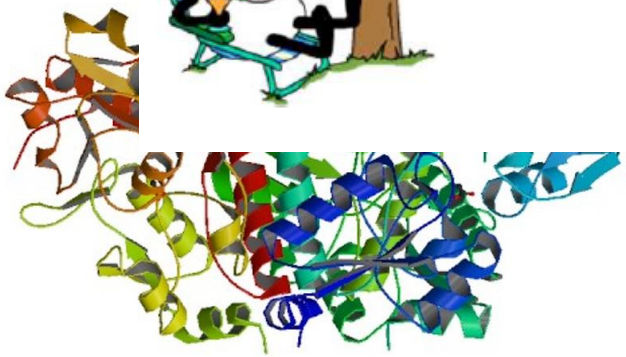
BB Xavier [1,2,3], C Lammens [1,2,3], R Ruhal [1,2,3], S Kumar-Singh [1,3,4], P Butaye [5,6,7], H Goossens [1,2,3], S Malhotra-Kumar [1,2,3]



DifferentTools To Improve Animal Health and Performance



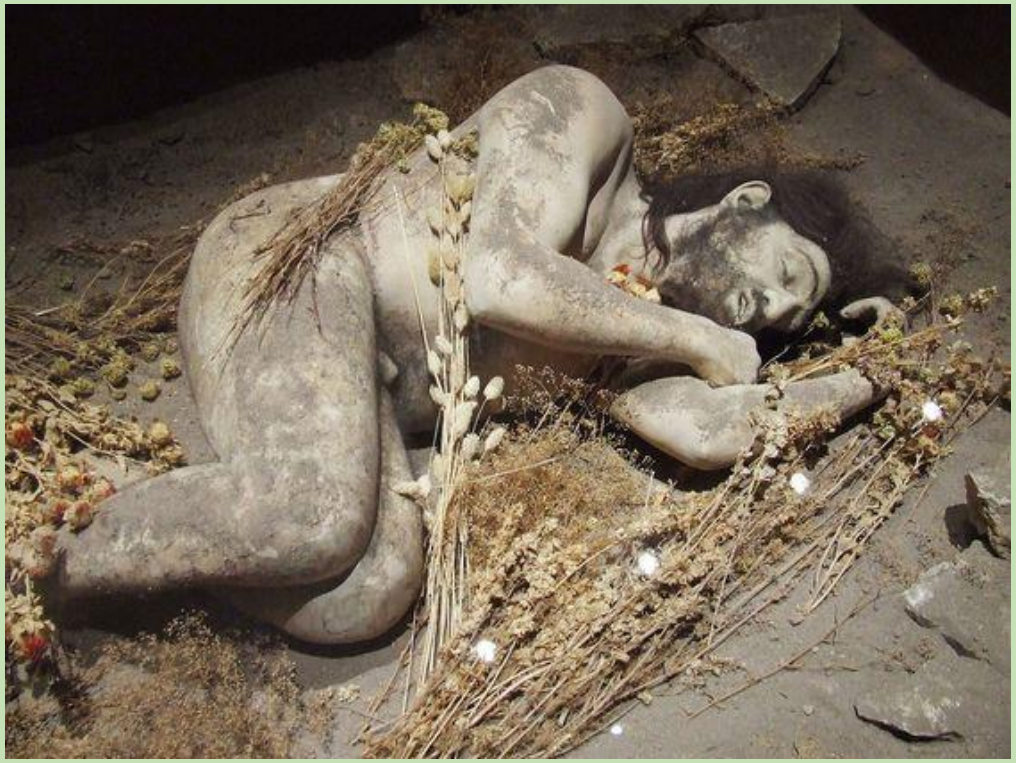




ORGANIC ACIDS

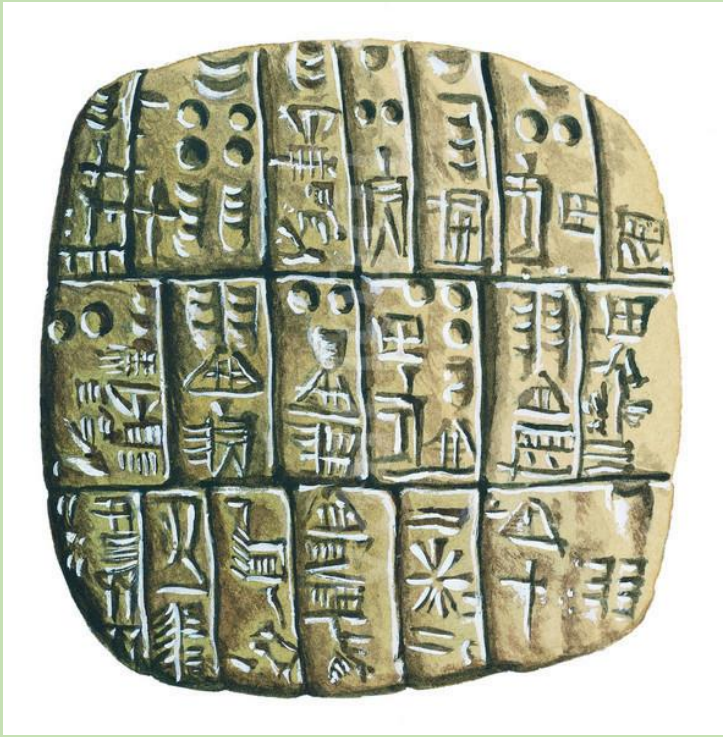
PREHISTORIC TIMES

- No one knows ……..
- Accidental discovery……. Pain…….folk knowledge
- Early evidence:
  - The grave of a Neanderthal man buried 60,000 years ago.
  - Pollen analysis indicated that plants buried with the corpse were all of medicinal value

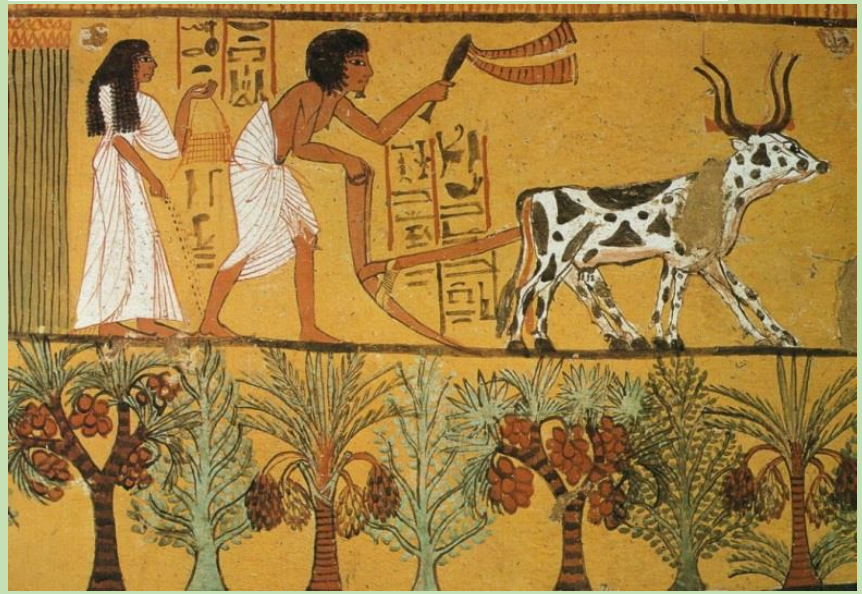


RECORDED HISTORY

- Earliest record 4,000 year old Sumerian clay tablet recorded numerous plant remedies



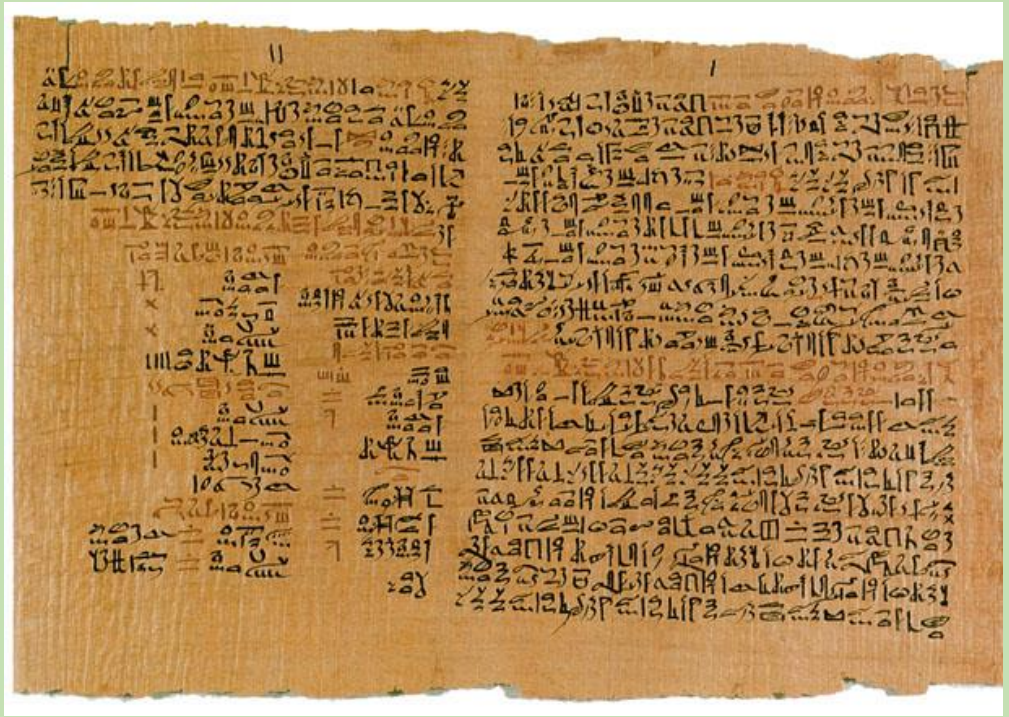
- Ancient Egyptian civilization left a wealth of information on medicinal plants and medical practice



ANCIENT EGYPT

- Wealth of knowledge in medicine
- Physicians highly respected and very specialized
- Several important medical papyri
  - **Ebers Papyrus**

- From 1550 B.C. one of the oldest
- Most important and complete medical papyrus recovered
- Hieratic script (similar to hieroglyphics)
- 20.23 m in length and 30 cm. in height
- 110 pages scroll contains 700 magical formulas and folk remedies



AUGUST 15, 2018

Prehistoric mummy reveals ancient Egyptian embalming 'recipe' was around for millennia

by University of York

Using chemical analysis, the scientific team led by the Universities of York and Macquarie uncovered evidence that the mummy had in fact undergone an embalming process, with a plant oil, heated conifer resin, an aromatic plant extract and a plant gum/sugar mixed together and used to impregnate the funerary textiles in which the body was wrapped.

This 'recipe' contained antibacterial agents, used in similar proportions to those employed by the Egyptian embalmers when their skill was at its peak some 2,500 years later.

ANCIENT CHINA

- The Pun-tsao, a pharmacopoeia published around 1600
- Contained thousands of herbal cures that are attributed to the works of Shen-nung, China's legendary Emperor who lived 4500 years ago
- Emperor Shen-nung investigated the medicinal value of several hundred herbs
- Knowledge passed on orally for centuries
- Use of *Ephedra* for asthma one of these

ANCIENT INDIA

- Herbal medicine dates back several thousand years to the Rig-Veda, the collection of Hindu sacred verses
- This is the basis of a health care system known as Ayurvedic medicine
- One useful plant that has come from Ayurvedic tradition is snakeroot, *Rauwolfia serpentina*

OLD WINE IN NEW BOTTLE

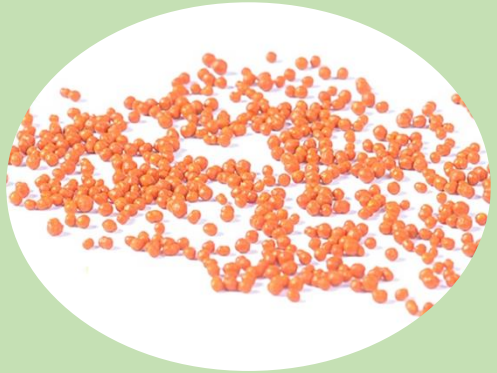
PLANT EXTRACTS AS FEED ADDITIVES IN ANIMAL PRODUCTION

- Naturally occurring bioactive plant compounds (plant extracts)
- Have properties designed to protect plant of origin
  - Antibacterial
  - Antifungal
- Used for years in traditional medicine & for food preservation
- Agriculture: High Potential to use as natural pesticide
- Food- To replace different chemicals
- Animal Health and Nutrition
  - Treatment or prevention of bacterial infection, parasites
  - Reduce the use of AGPs
  - Intestinal Health, Immune response and other health issues

ESSENTIAL OIL BLEND- WHAT WE KNOW?

- **Always recommended to use blend of EO**
- **Well documented synergic effect between different EO**
- **Effect at gene level at low inclusion**
- **Gene to gene interaction**

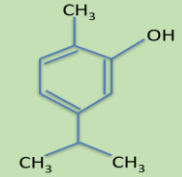
ESSENTIAL OIL BLEND- WHAT WE KNOW?



Plant essential oil

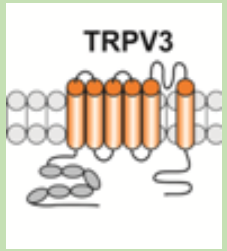
Oregano

Active



Carvacrol

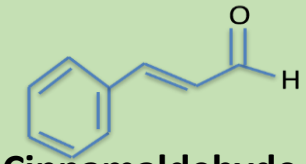
Intestinal receptor



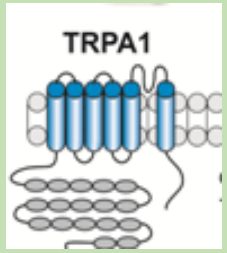
Animal response

↓ inflammation

Cinnamon

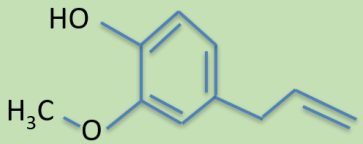


Cinnamaldehyde

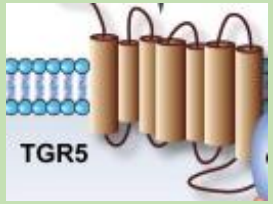


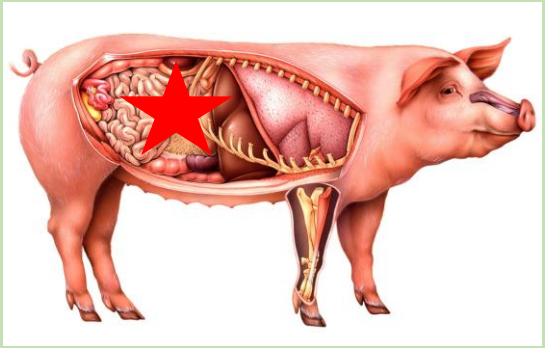
↑ nutrient absorption

Clove



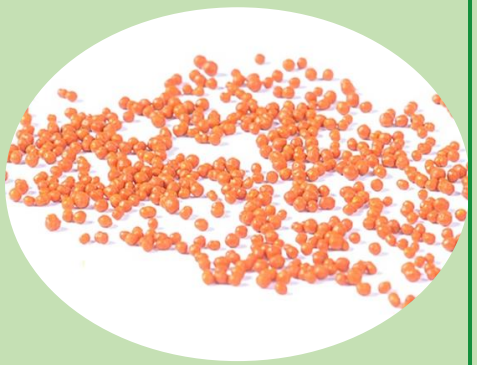
Eugenol





↑ intestinal integrity

ESSENTIAL OIL BLEND- WHAT WE KNOW?



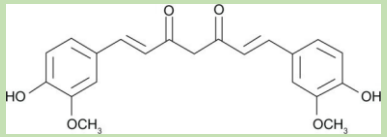
Plant/EO/OR

Active

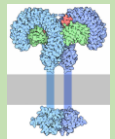
Intestinal receptor

Animal response

Turmeric Oleoresin



Curcumin

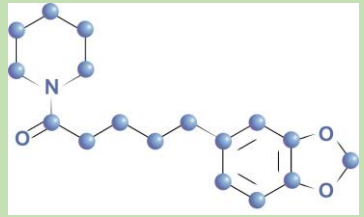


TLR-4

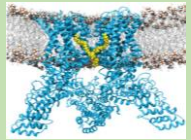
NFk-B
MAP-K
Inflammation

PPAR-γ

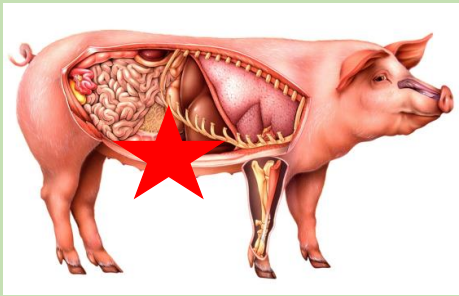
Lymphocytes
Phagocytosis
Antibody production



Piperine

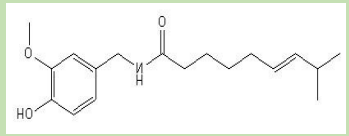


TRPV-1

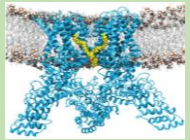


Inflammation

Capsicum oleoresin

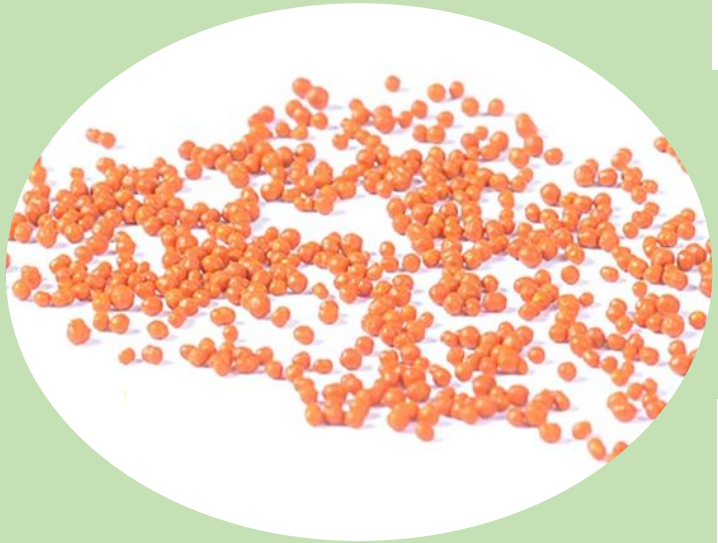


Capsacinoids

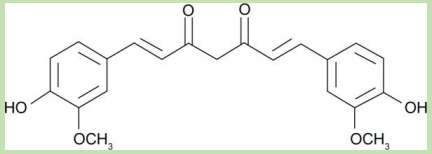


TRPV-1

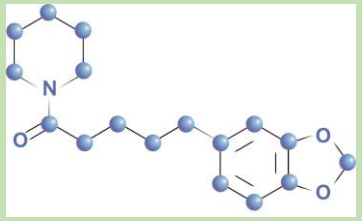
COMBINATION OF PIPERINE WITH CURCUMIN



Turmeric Oleoresin



Curcumin

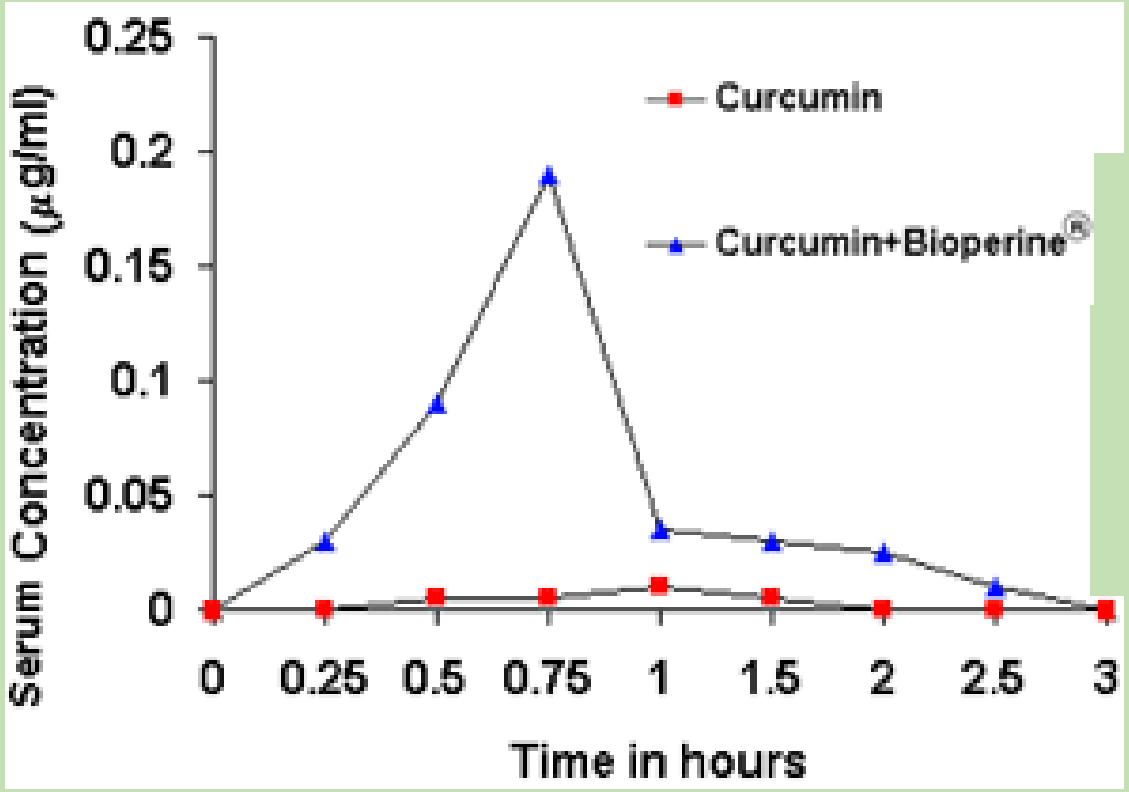


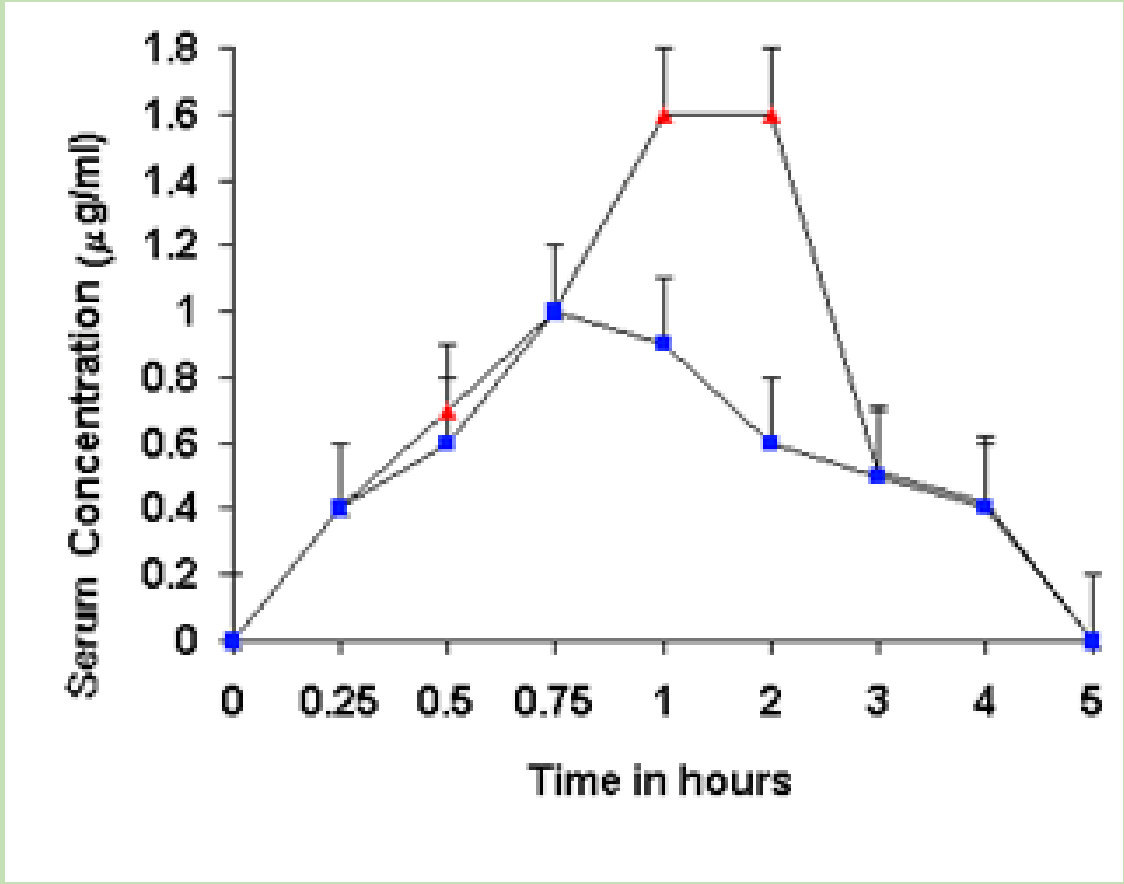
Piperine

- Bioavailability enhancer
- Major active component of black pepper
- Is associated with an increase of in the bioavailability of curcumin

Planta Med 1998; 64(4): 353-356

PIPERINE INCREASES CURCUMIN BIOAVAILABILITY





Planta Med 1998; 64(4): 353-356

Plant extract based Additives- what the future holds in its hands?

Food Chemistry 119 (2010) 1346–1351

Contents lists available at Scie

Food Chemist

journal homepage: www.elsevier.co

Curcumin inhibits influenza virus infection and

Da-Yuan Chen [a], Jui-Hung Shien [b], Laurence Tiley [c], Shyan-Sor
Tien-Jye Chang [b], Ya-Jane Lee [b,e], Kun-Wei Chan [b], Wei-Li Hsu

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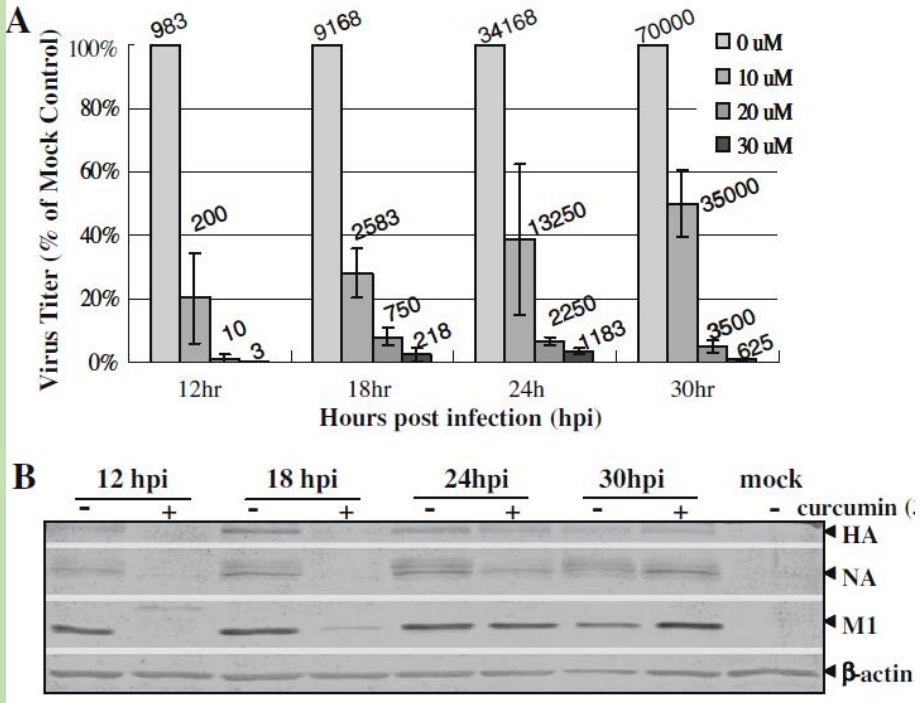

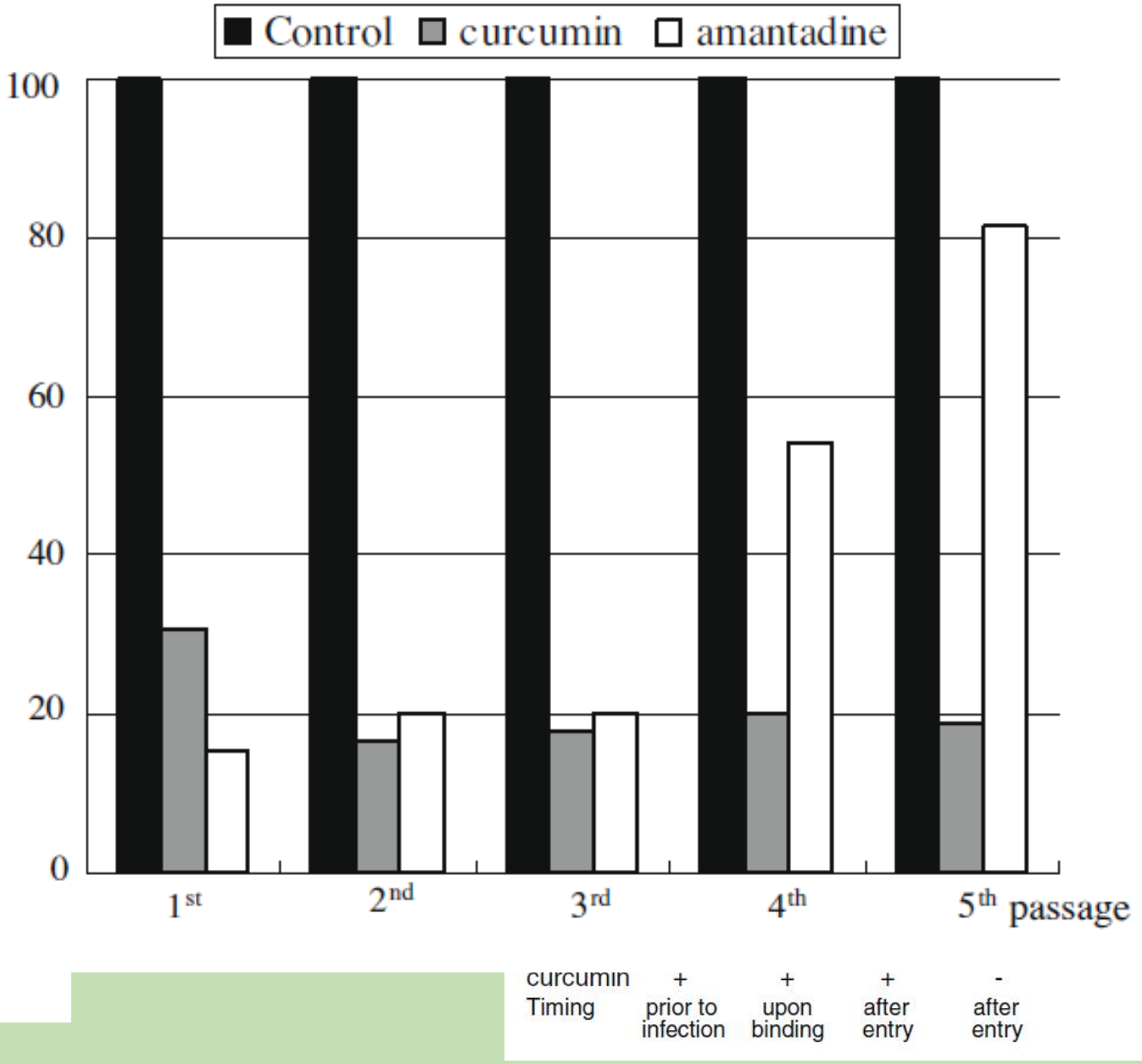

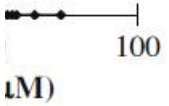

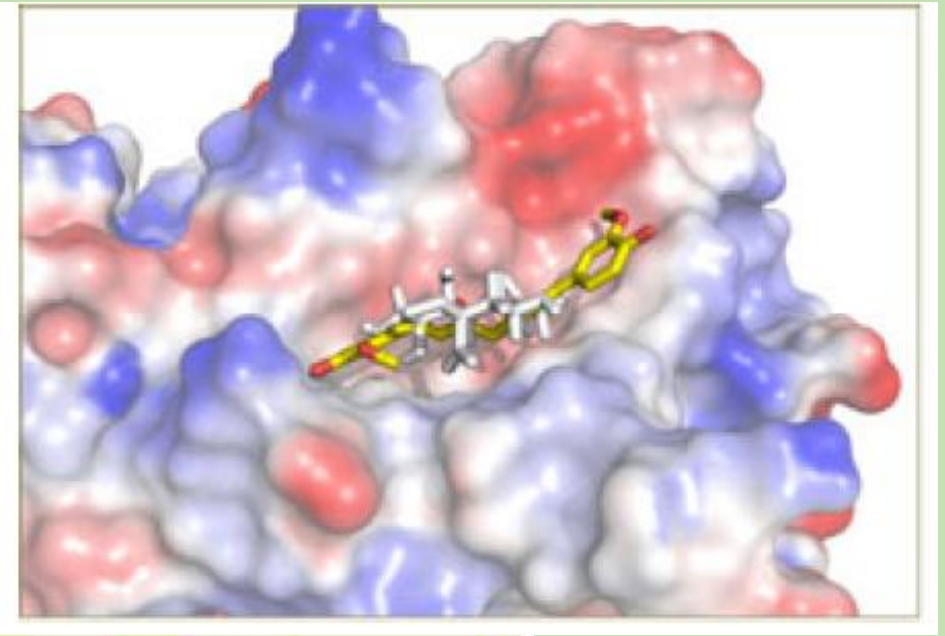

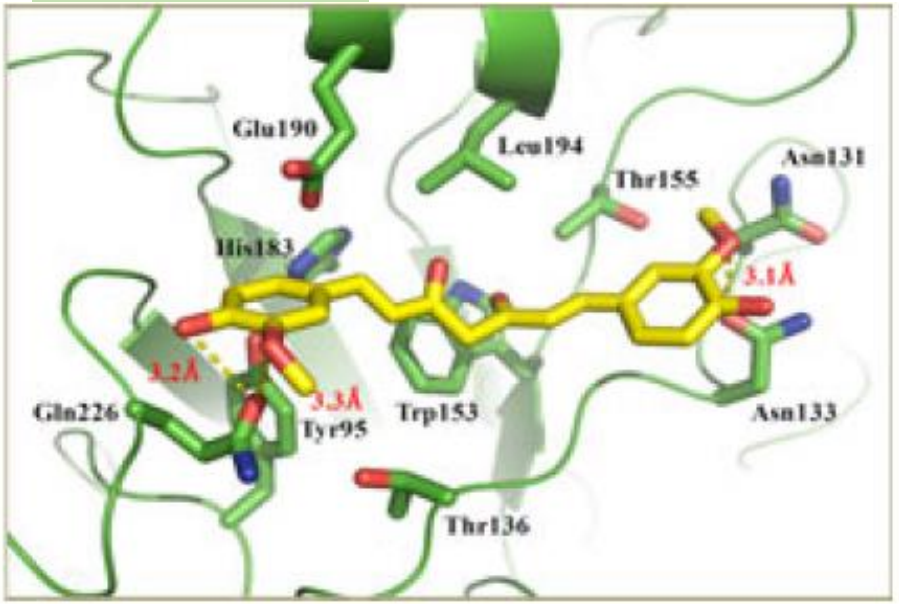

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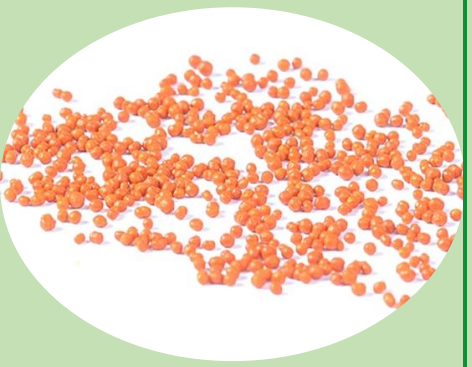
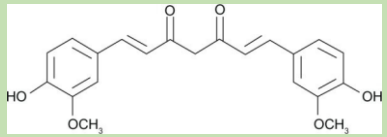
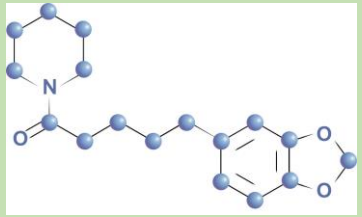
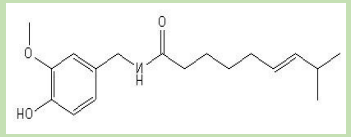
COMMERCIAL TRIAL



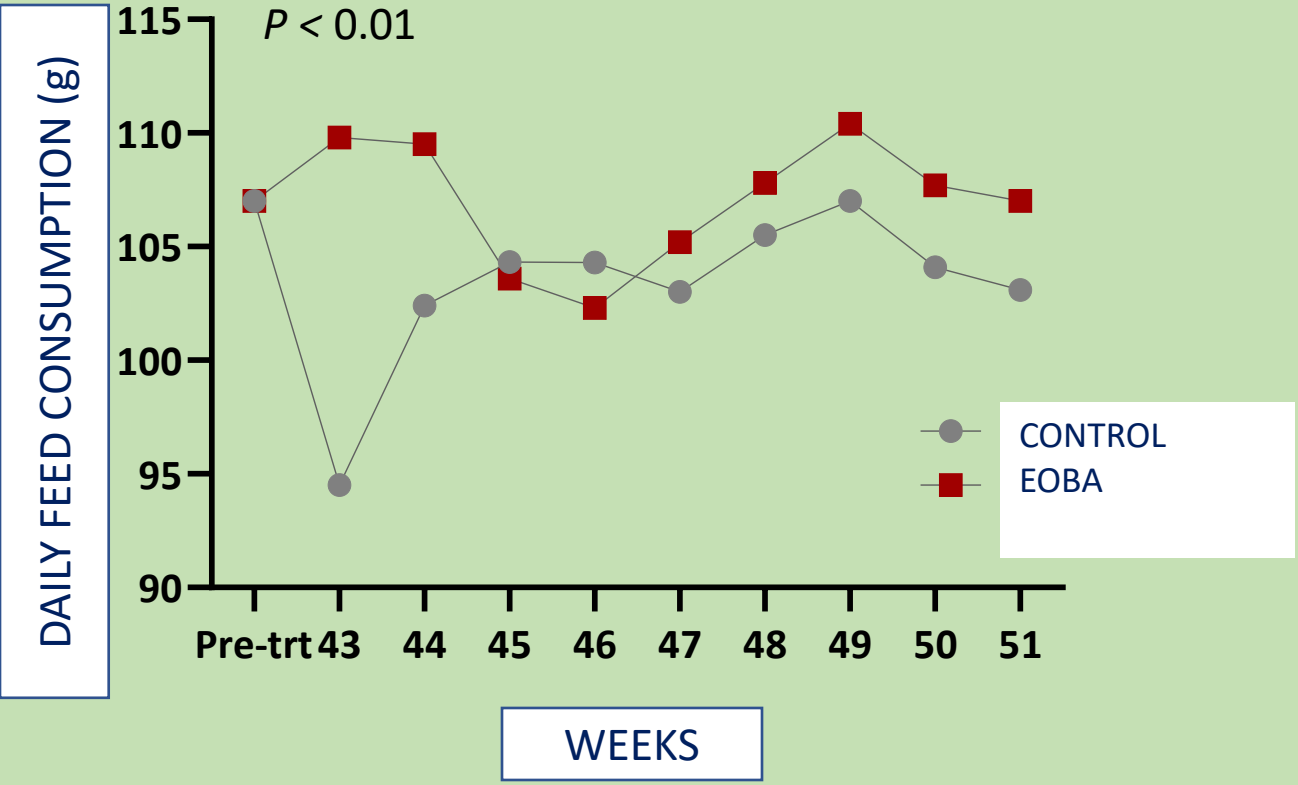
Plant/EO/OR	Active
 Turmeric Oleoresin	 Curcumin
	 Piperine
 Capsicum oleoresin	 Capsacinoids

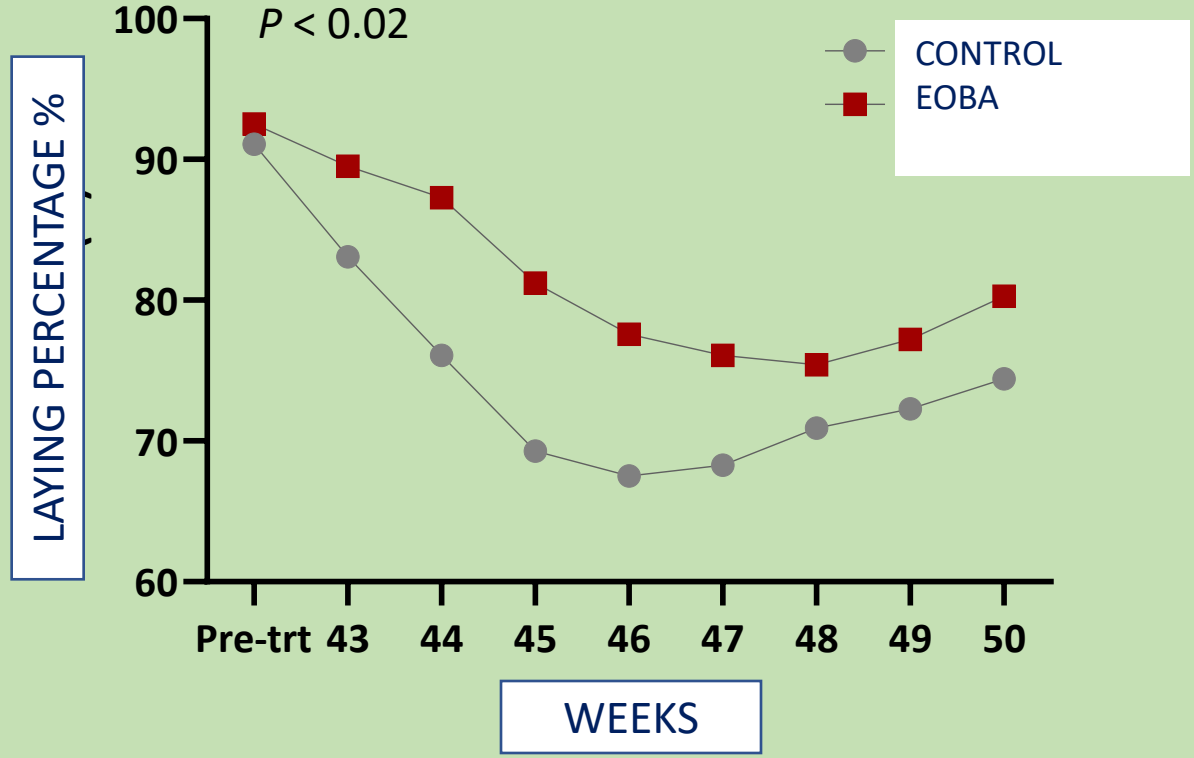
AGE OF THE BIRDS 43 WEEKS

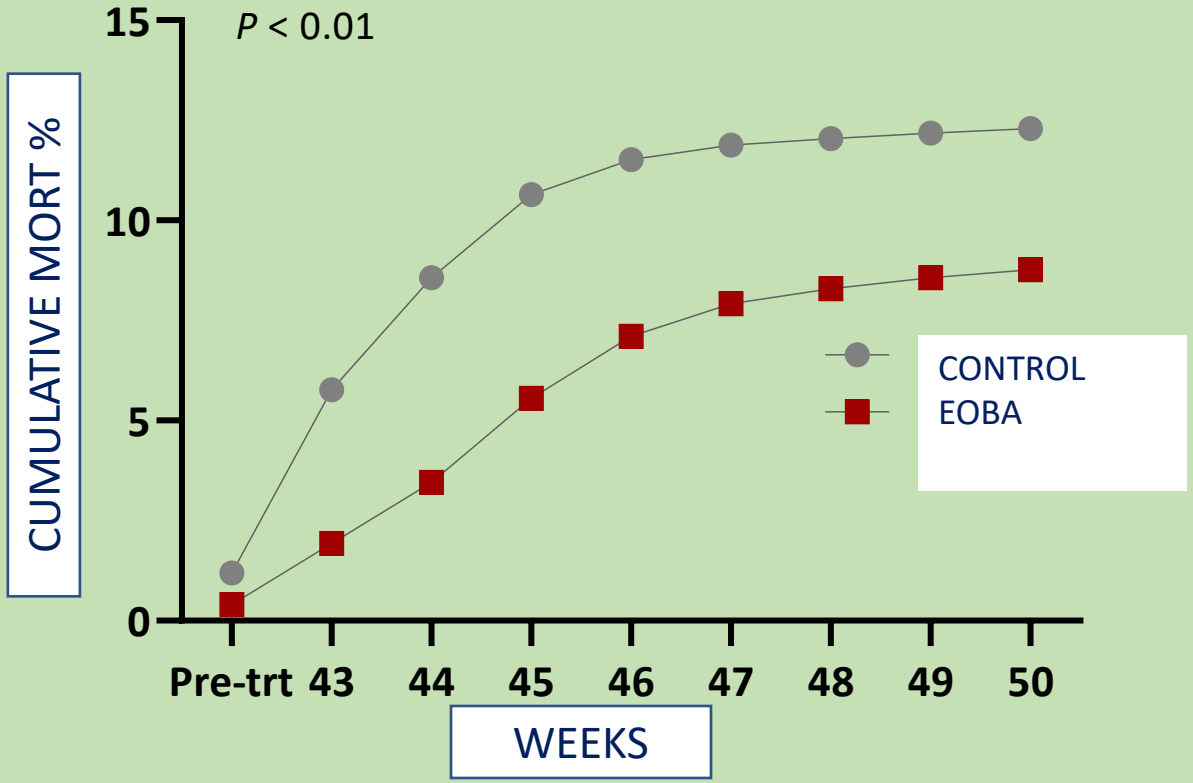
CONTROL AND EXPERIMENTAL GROUP

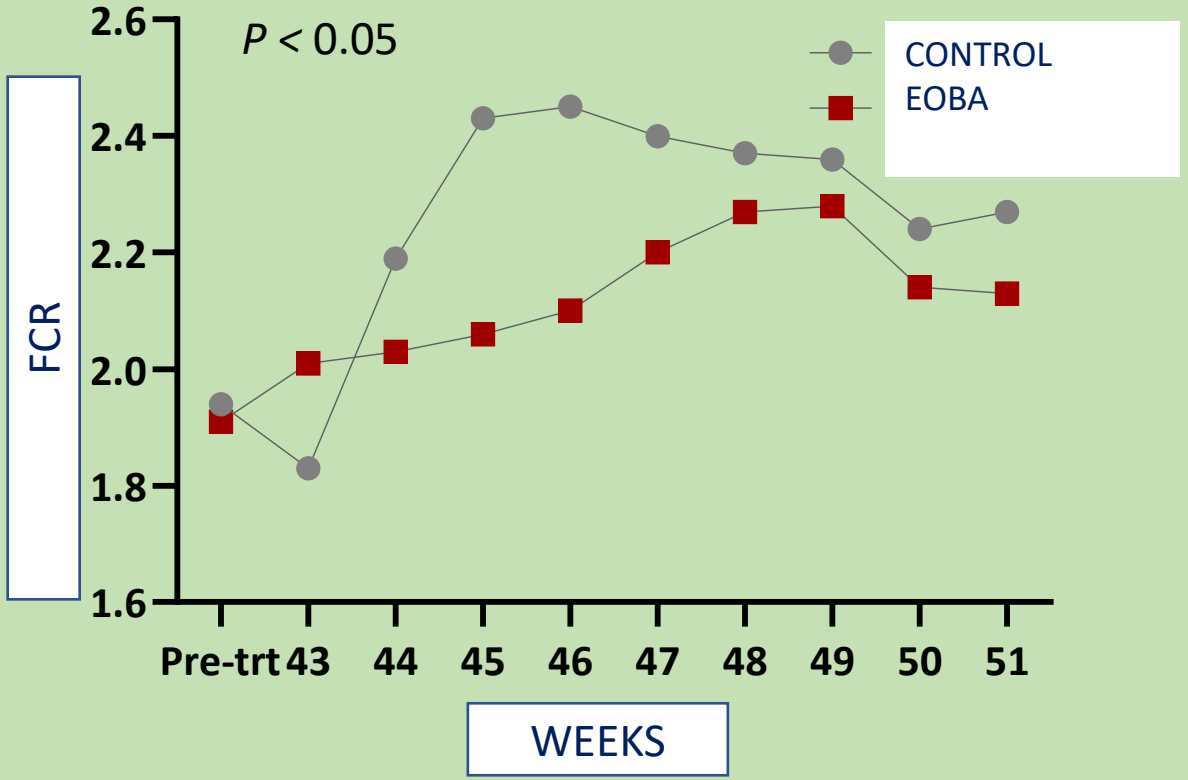
60,000 LAYERS PER GROUP

BOTH THE GROUPS WERE INFECTED

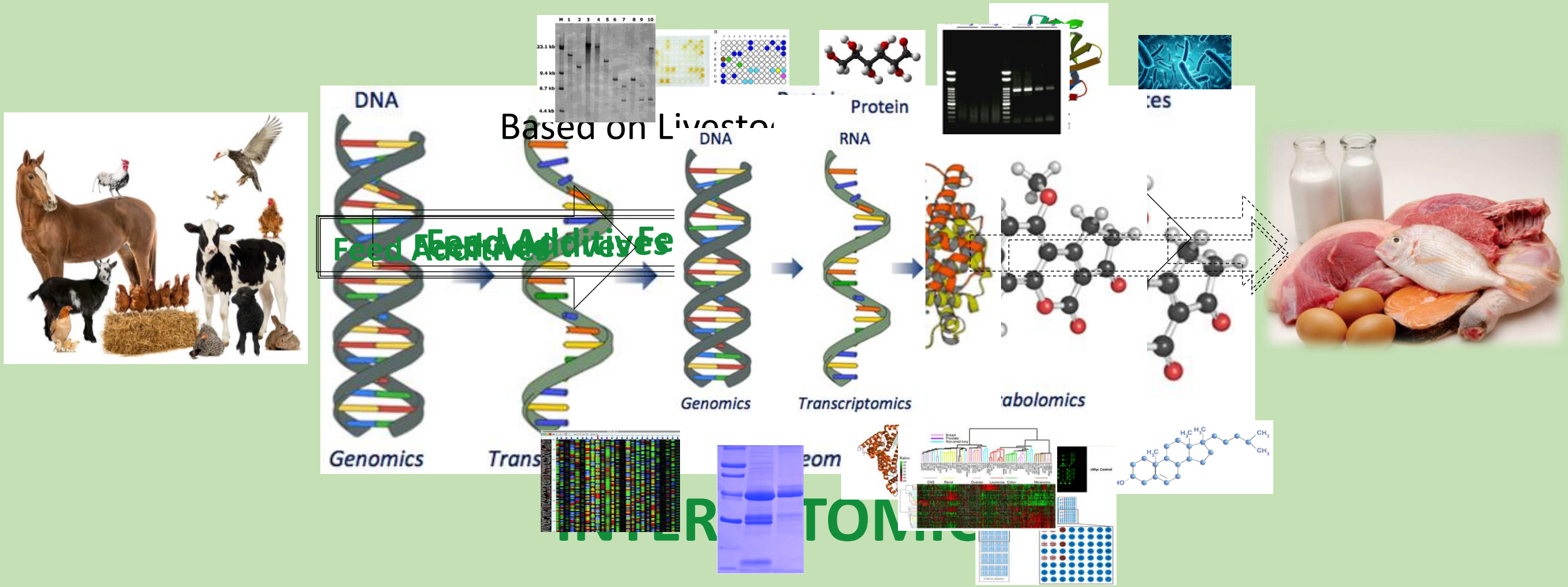

DAILY FEED CONSUMPTION (g)
P < 0.01
115
110
105
100
95
90
Pre-trt 43 44 45 46 47 48 49 50 51
CONTROL
EOBA
WEEKS


LAYING PERCENTAGE %
P < 0.02
100
90
80
70
60
Pre-trt 43 44 45 46 47 48 49 50
CONTROL
EOBA
WEEKS

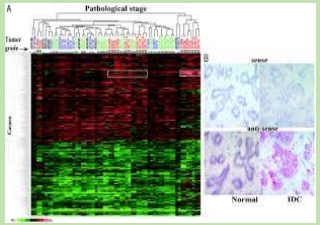

P < 0.01
CUMULATIVE MORT %
15
10
5
0
Pre-trt
43
44
45
46
47
48
49
50
WEEKS
CONTROL
EOBA


P < 0.05
FCR
2.6
2.4
2.2
2.0
1.8
1.6
Pre-trt
43
44
45
46
47
48
49
50
51
WEEKS
CONTROL
EOBA

PLANT EXTRACT BASED ADDITIVES- WHAT THE FUTURE HOLDS IN ITS HANDS?

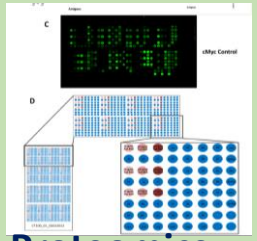


INTERACTOMICS & PHYTOGENIC FEED ADDITIVES

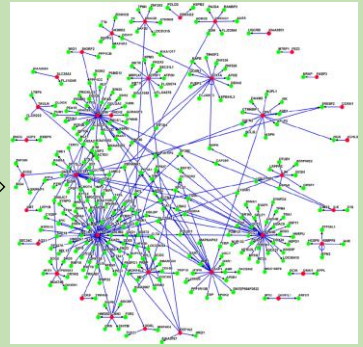


Nutrigenomics

PhytoGenics

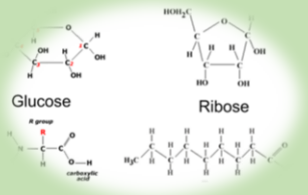


Proteomics



Systems Biology - Interactomics

- Molecular Mechanism of action
- Cumulative effect
- Cross reactivity/ Adverse Effects
- Alternate applications



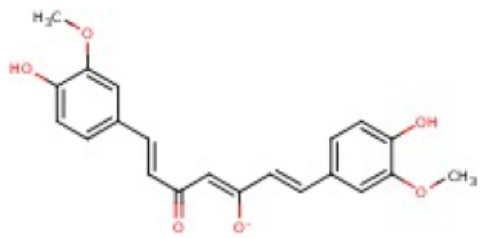
Metabolomics

PLANT EXTRACT BASED ADDITIVES- WHAT THE FUTURE HOLDS IN ITS HANDS?

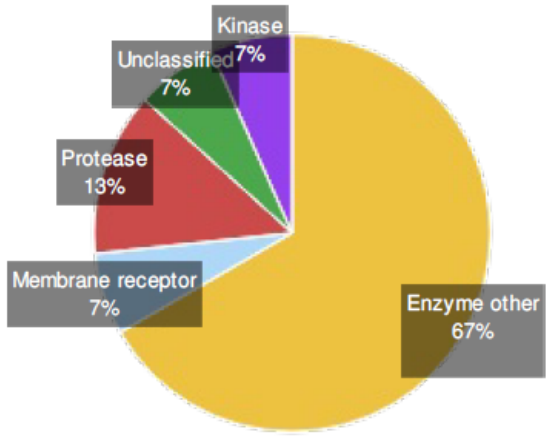
SwissTargetPrediction report:

Reference:
Gfeller D., Michielin O. & Zoete V. Shaping the interaction landscape of bioactive molecules, *Bioinformatics* (2013) 29:3073-3079.

Query Molecule



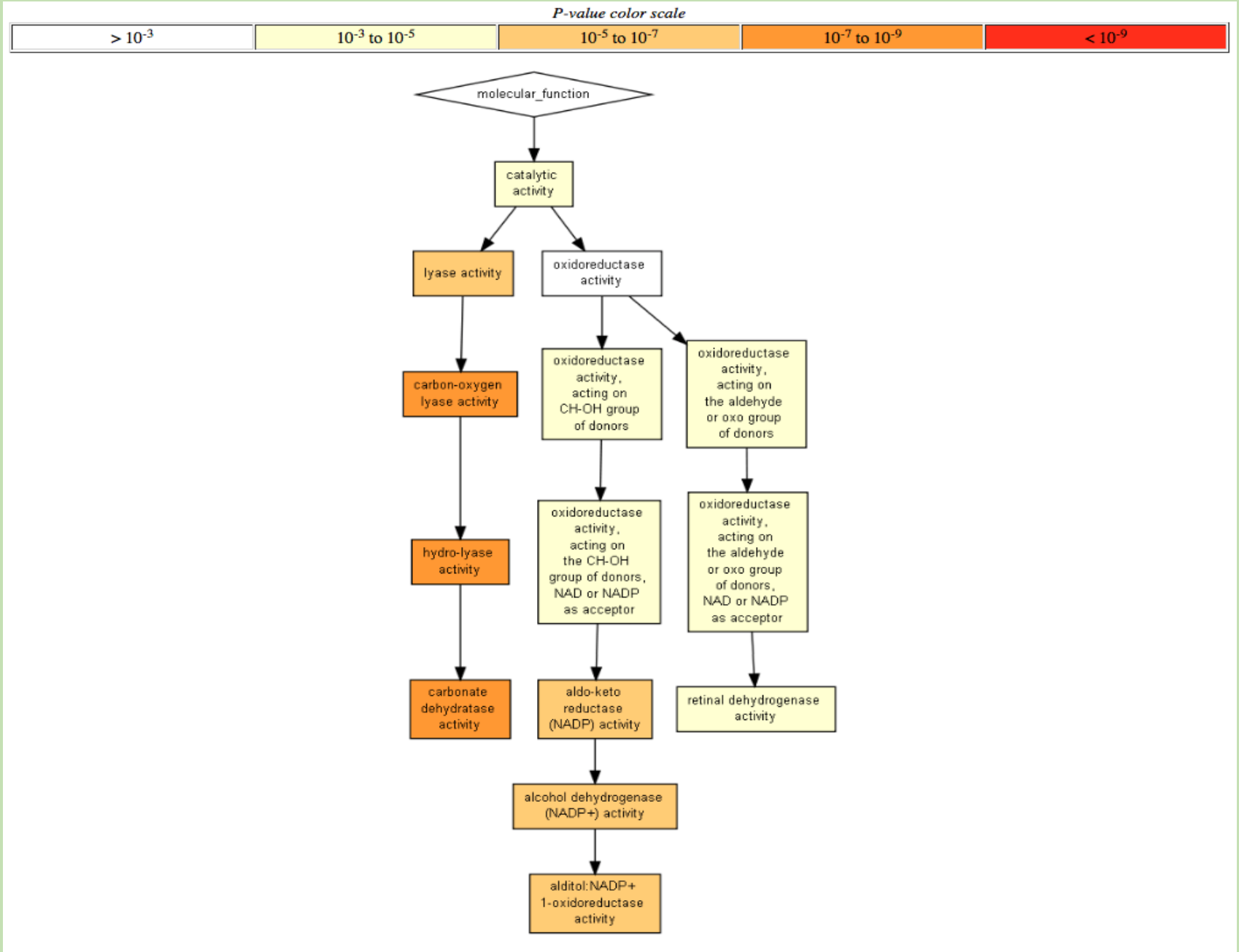
Frequency of Target Class



Target	Uniprot ID	Gene code	ChEMBL ID	Probability	# sim. cmpds (3D / 2D)	Target Class
Carbonic anhydrase 12	O43570	CA12	CHEMBL3242		6 / 6	Enzyme
Carbonic anhydrase 1	P00915	CA1	CHEMBL261		34 / 7	Enzyme
Carbonic anhydrase 2	P00918	CA2	CHEMBL205		34 / 7	Enzyme
Gamma-secretase C-terminal fragment 59	P05067	APP	CHEMBL2487		2 / 12	Membrane receptor
Carbonic anhydrase 3 *(by homology)*	P07451	CA3	CHEMBL2885		34 / 7	Enzyme
PEX *(by homology)*	P08253	MMP2	CHEMBL333		15 / 2	Metallo Protease
Arachidonate 5-lipoxygenase	P09917	ALOX5	CHEMBL215		1 / 11	Enzyme
Microtubule-associated protein tau	P10636	MAPT	CHEMBL1293224		2 / 43	Unclassified
67 kDa matrix metalloproteinase-9	P14780	MMP9	CHEMBL321		15 / 2	Metallo Protease
Carbonic anhydrase 4	P22748	CA4	CHEMBL3729		20 / 2	Enzyme
Prostaglandin G/H synthase 1	P23219	PTGS1	CHEMBL221		2 / 9	Enzyme
Carbonic anhydrase 6	P23280	CA6	CHEMBL3025		1 / 4	Enzyme
Protein kinase C eta type *(by homology)*	P24723	PRKCH	CHEMBL3616		3 / 2	Ser_Thr Kinase
Carbonic anhydrase 5A, mitochondrial *(by homology)*	P35218	CA5A	CHEMBL4789		34 / 7	Enzyme
Nitric oxide synthase, inducible	P35228	NOS2	CHEMBL4481		1 / 5	Enzyme

EFFECT OF CURCUMIN ON DIFFERENT PHYSIOLOGICAL PROCESSES

CURCUMIN-MOLECULAR FUNCTION



CONCLUSION

- The use of Phytogenics for improving Health is an Ancient Concept.
- Studies in production animals show that traditional medicine applies to them as well.
- The application of novel modern technologies to this ancient practice Will allow for clarified mechanisms, refined applications
- New concepts to address challenged in animal production