



How Phenolic Based Compounds can be increase productivity in the Pharmaceutical Industry

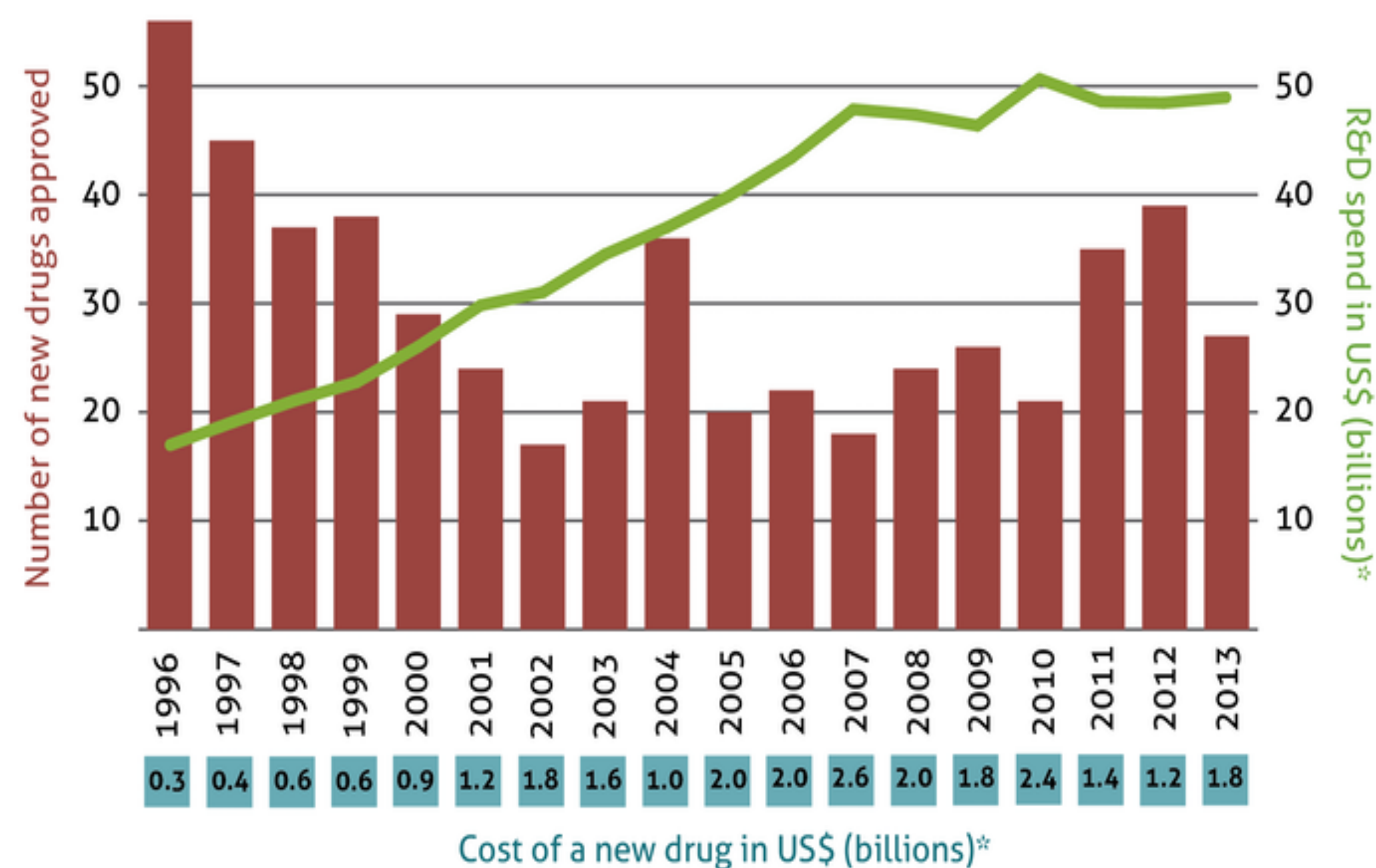
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Introduction/Background

- In recent years, the cost of developing drugs has increased immensely. Many drugs created and produced has cost upwards of 2 billion dollars, with the majority of the funds being devoted to the discovery of new pharmaceuticals¹
- The time to develop a New Drug Entity (NDA) has increased significantly, taking more than a decade now
- The number of new drugs made, the productivity of the pharmaceutical industry, has shown a downward trend
- Currently, over 50% of pharmaceuticals require the use of three palladium catalyzed reaction: Sonogashira Coupling, Suzuki Coupling and Heck Reaction
- This Study compares Phenolic medicinal compounds in comparison to traditional produced pharmaceuticals to advocate for more research and development into Phenolic compounds to help increase the productivity of the pharmaceutical industry

Productivity of the pharma industry

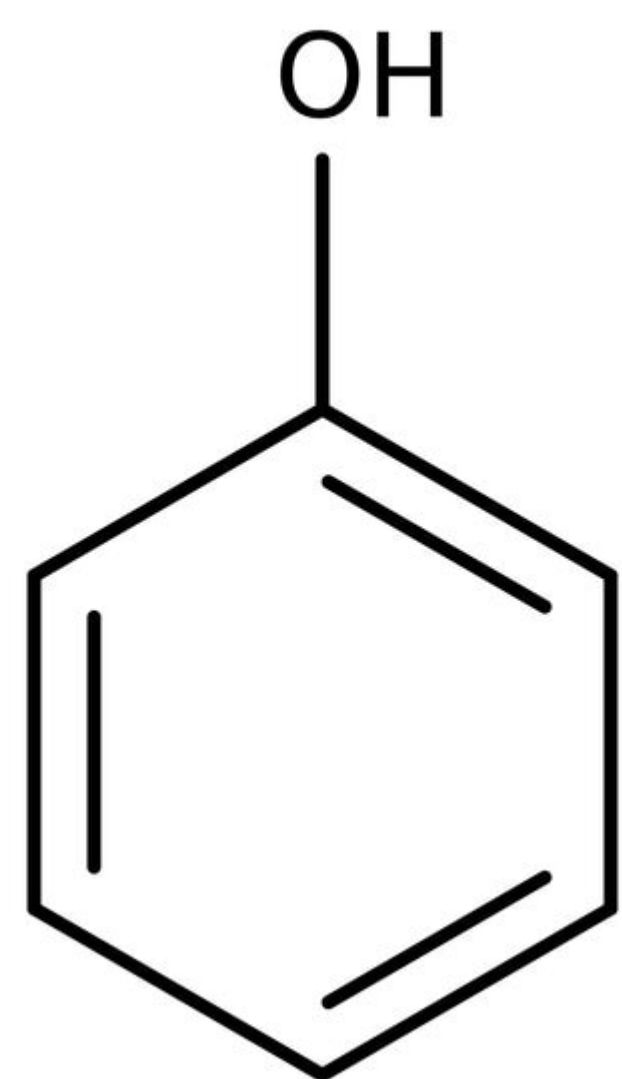
Finding the true cost of a new drug is complex and controversial...



The decreasing productivity of the pharmaceutical industry²

Phenolic Compounds

- These compounds contain a phenol functional group and at least one hydroxyl group
- Ubiquitous in many sources of energy for humans (plants and animal meat)
- Act as good antioxidants due to the prevalence of hydroxyl groups
- High diversity of structures outside of the base compounds and are have a low toxicity

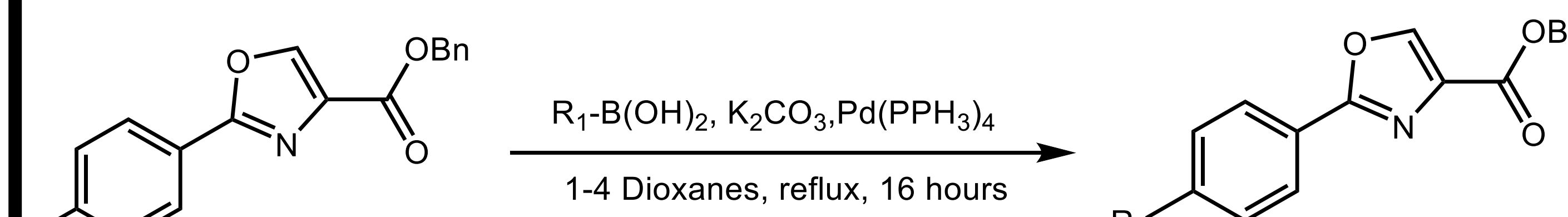


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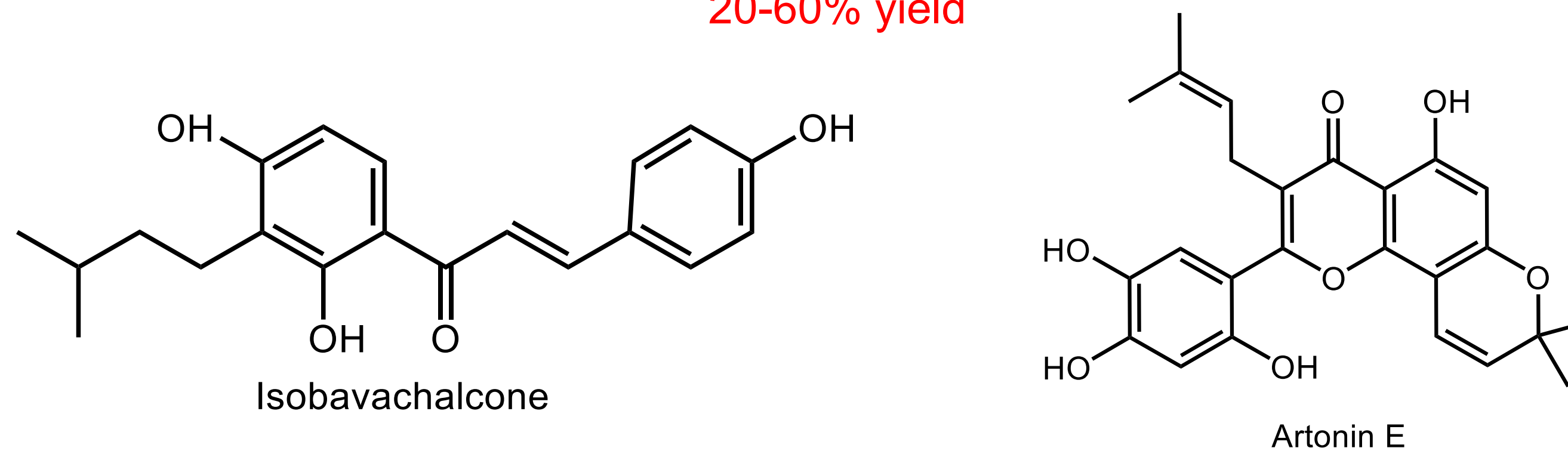
Comparison Analysis

- Drugs derived from Phenolic compounds were directly compared to comparable pharmaceuticals created by traditional means



Potent Anti-TB analogs based on a general oxazole benzyl ester core³

20-60% yield

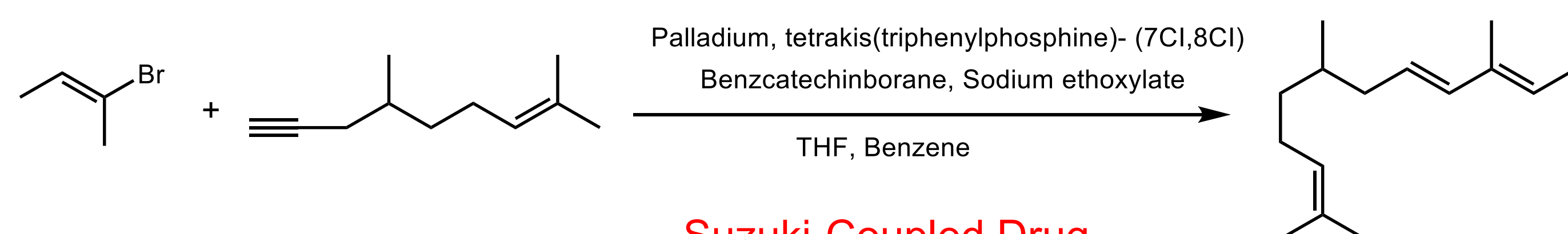


Anti-TB drugs derived from Phenolic Compounds⁴

99% concentration

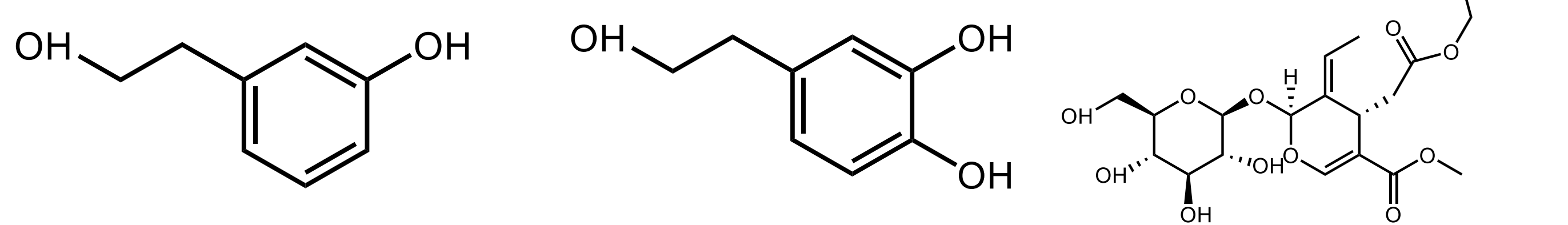
Anti-TB Pharmaceuticals

- Phenolic based compounds demonstrated a comparable performance to traditional produced compounds due to the strong antioxidant nature of the compounds⁴
- Isobavchalcone and Artonin E are much easier to concentrate due to them being found in common plants such as Monkey Fruit
- Due to their sources being common plants, Isobavachalcone and Artonin E are easier to obtain



Suzuki-Coupled Drug

Caparratriene⁵
36% yield



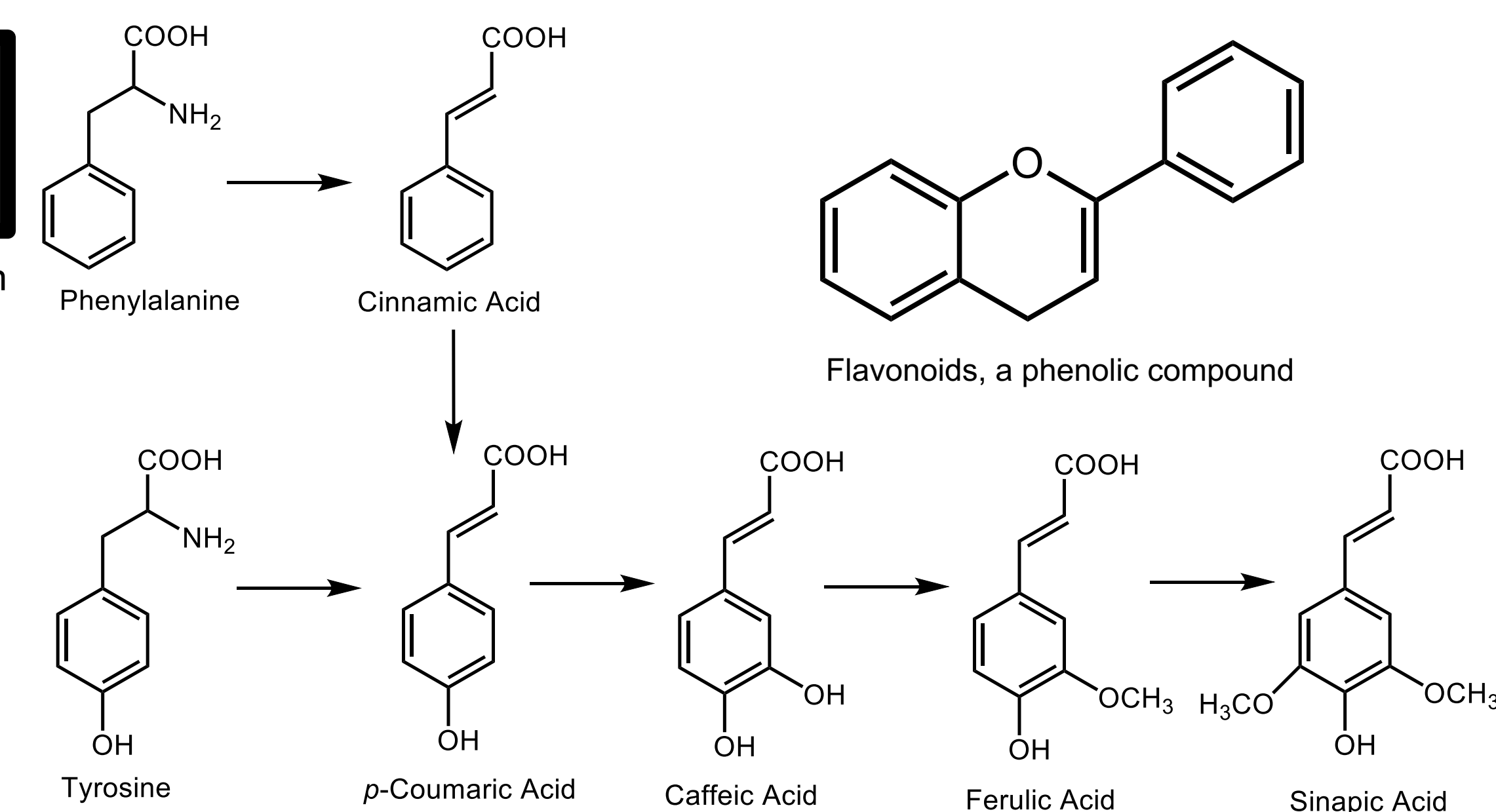
Tyrosol
14% concentration

Hydroxytyrosol
14% concentration

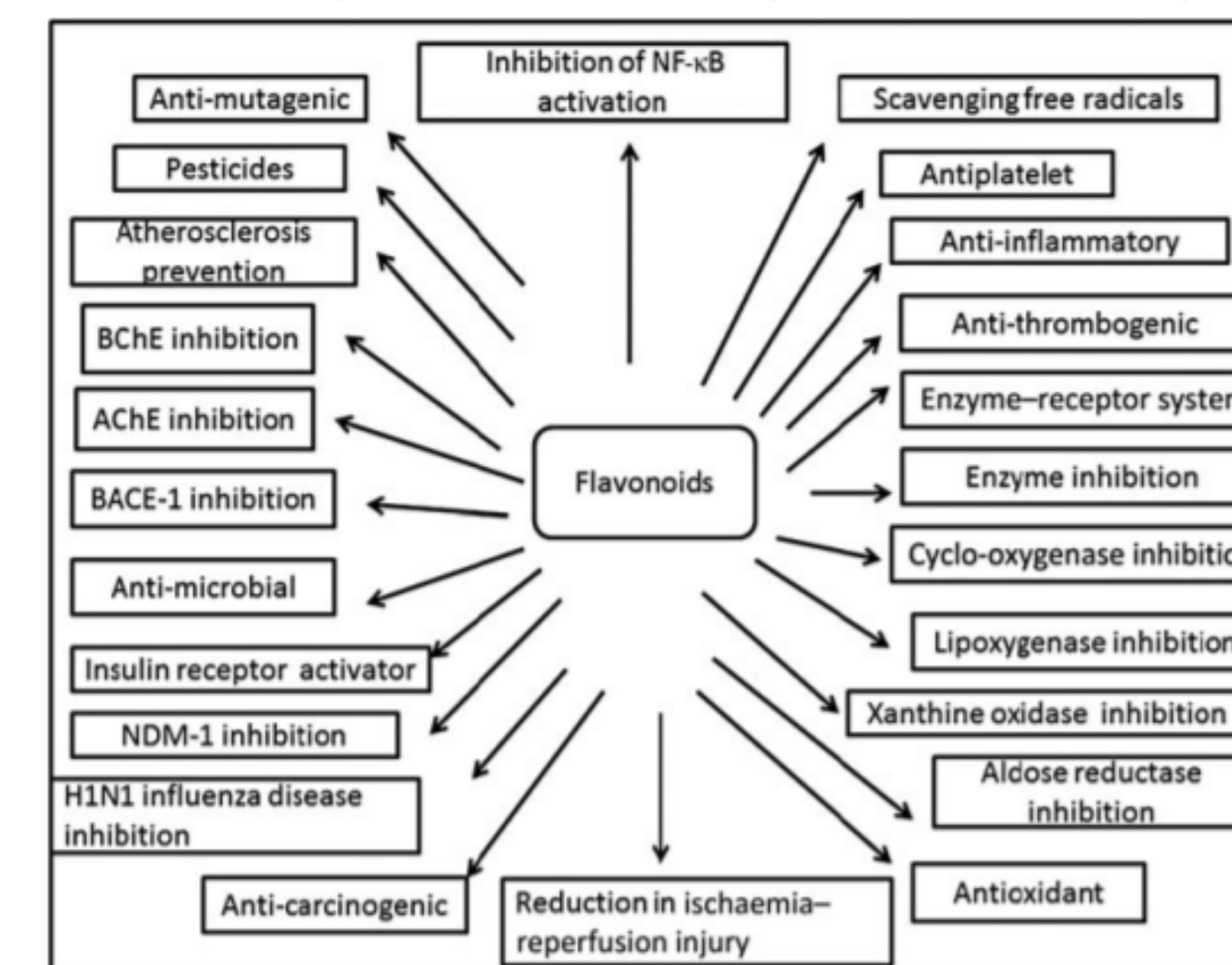
Oleuropein
19% concentration

Anti-Leukemia Pharmaceuticals

- Tyrosol, Hydroxytyrosol and Oleuropein demonstrate anti-leukemia properties in their unrefined form due to the high number of hydroxyl groups^{7,8}
- Have the capability to be synthetically created and further modified far beyond their original structure
- Although they have lower concentrations than the yield of Caparratriene, the fact that all of the Phenolic compounds are found in olive oil far decreases their costs when compared to Caparratriene



Creation of a complex Phenolic compound from a simple one



Medicinal Uses of Flavonoids, a Phenolic based compounds⁹

Overall Analysis

- Phenolic Medicinal Compounds display performance comparable due to the hydroxyl groups present in the compound
- Phenolic Compounds tend to be cheaper due to their prevalence in nature such as plants
- Phenols demonstrate a wide variety of uses and can be utilized against a vast array of diseases and conditions due to its immense diversity of structures
- Since Phenolic Compounds can be synthetically created, it allows scientists to not rely on deriving them from nature
- Their low toxicity, owing to them being found in many edible plants, gives them a step up in testing over traditionally produced compounds
- However, due to the structure of Phenolic Compounds, they have a low solubility and low bioavailability, necessitating the need of a carrier in the human body sometimes

Conclusions/Further Research

- Phenolic compounds represent a cost effective and under utilized group of molecules that have medicinal uses
- Given their lower cost of production and concentration, they can significantly reduce the overall cost of drug development
- They can decrease time spent in development as their low toxicity makes them more likely to succeed in clinical trials
- Phenolic compounds have the potential to vastly improve productivity in the pharmaceutical industry
- To make Phenolic compounds even more relevant, research can be taken in increasing their solubility and bioavailability