

BIOSYNTHESIS OF VARIN SERIES CANNABINOIDS

TEEWINOT LIFE SCIENCES CORPORATION

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Cann10 Conference

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Current Methods of Cannabinoid Manufacture

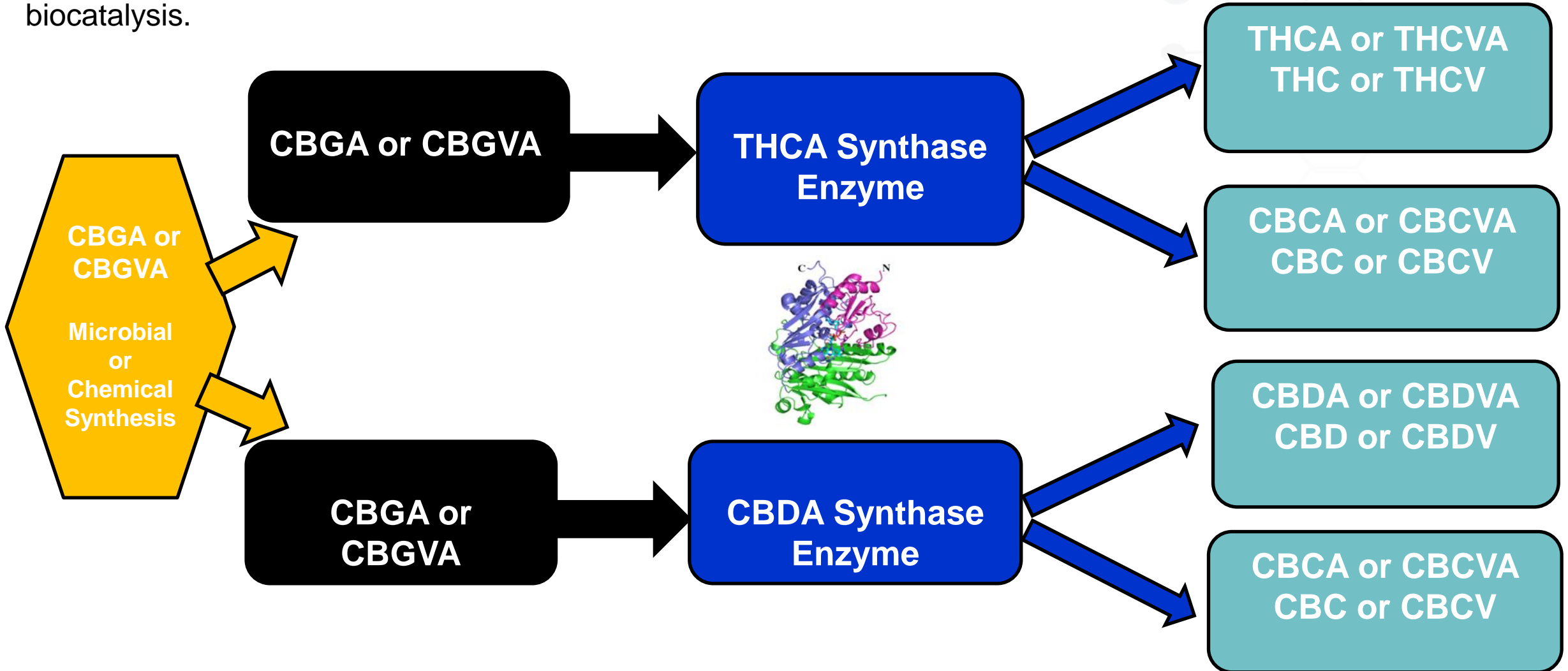
Plant Cultivation	Chemical Synthesis
Resource Intensive	Resource Intensive – Requires Development of Chiral Synthetic Strategies - Challenging and Needs Validation
Expensive	Expensive
Requires Months	Requires Days – Weeks
Plants Prone to Genetic Drift and Produce Very Low Quantities of Many Cannabinoids	
Purification and Dosing Challenges	Requires Development of Purification Methods for Producing Commercial Amounts of Pharmaceutical Grade Cannabinoid Compounds
Difficult QA/QC – FDA Issues	Detailed Structural Characterization and QA/QC data Required for FDA Approval

Teewinot's CannSynthesis™ Technology

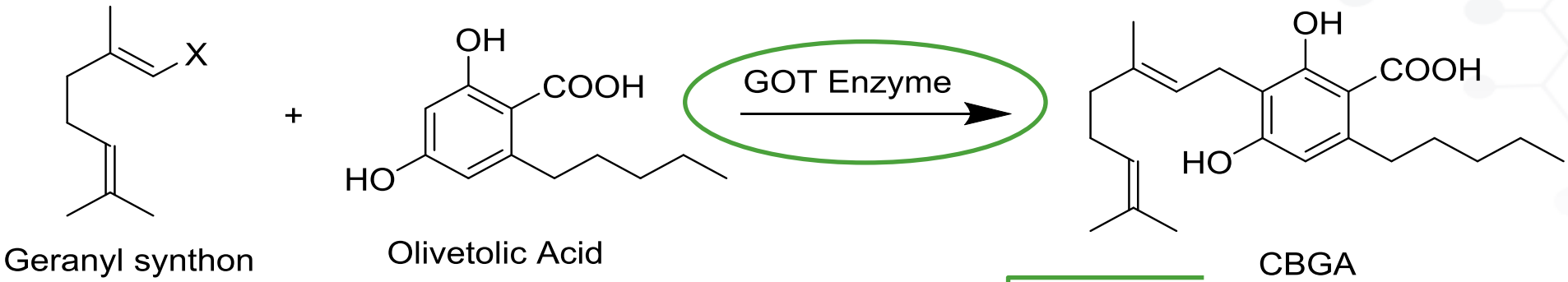


CannSynthesis™ Process Overview

Clone *Cannabis* genes coding for cannabinoid biosynthetic enzymes into a microorganism. Manufacture cannabinoids in microorganisms or using biocatalysis.



Production of CBGA or CBGVA in Microorganisms

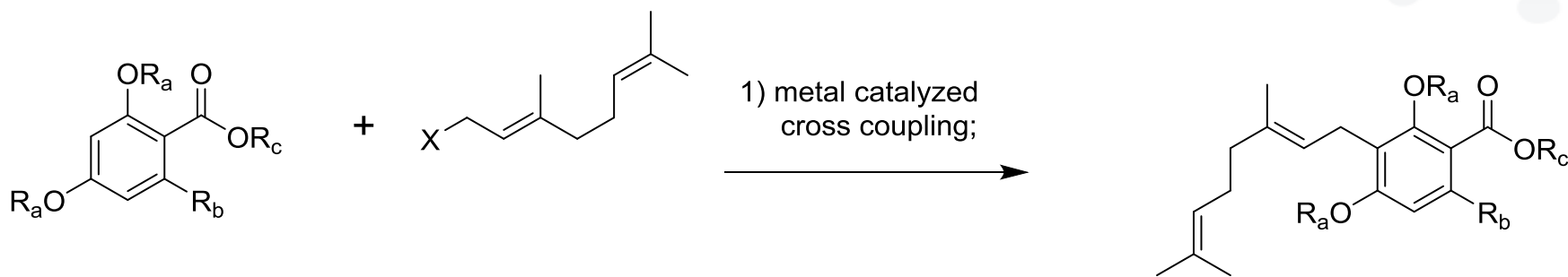


II. Cannabinoid Production

THCA Synthase
CBDA Synthase



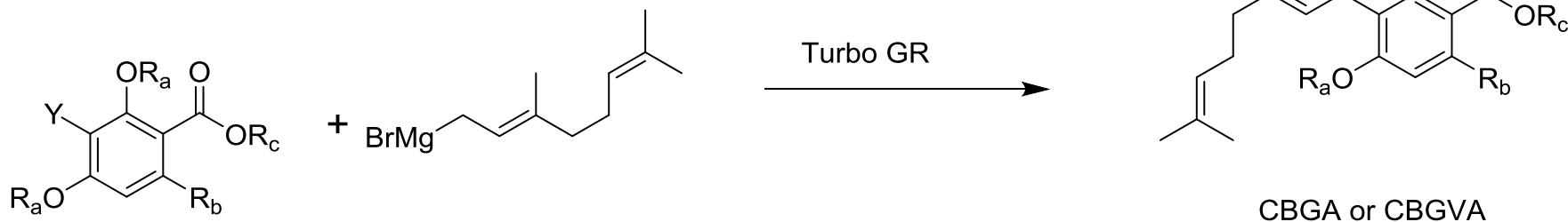
Chemical Synthesis of CBGA or CBGVA



R_a = H, PG
 R_b = alkyl, or an appropriate substituent;
 R_c = ester forming group

X = leaving group

CBGA or CBGVA



Y = reactive group

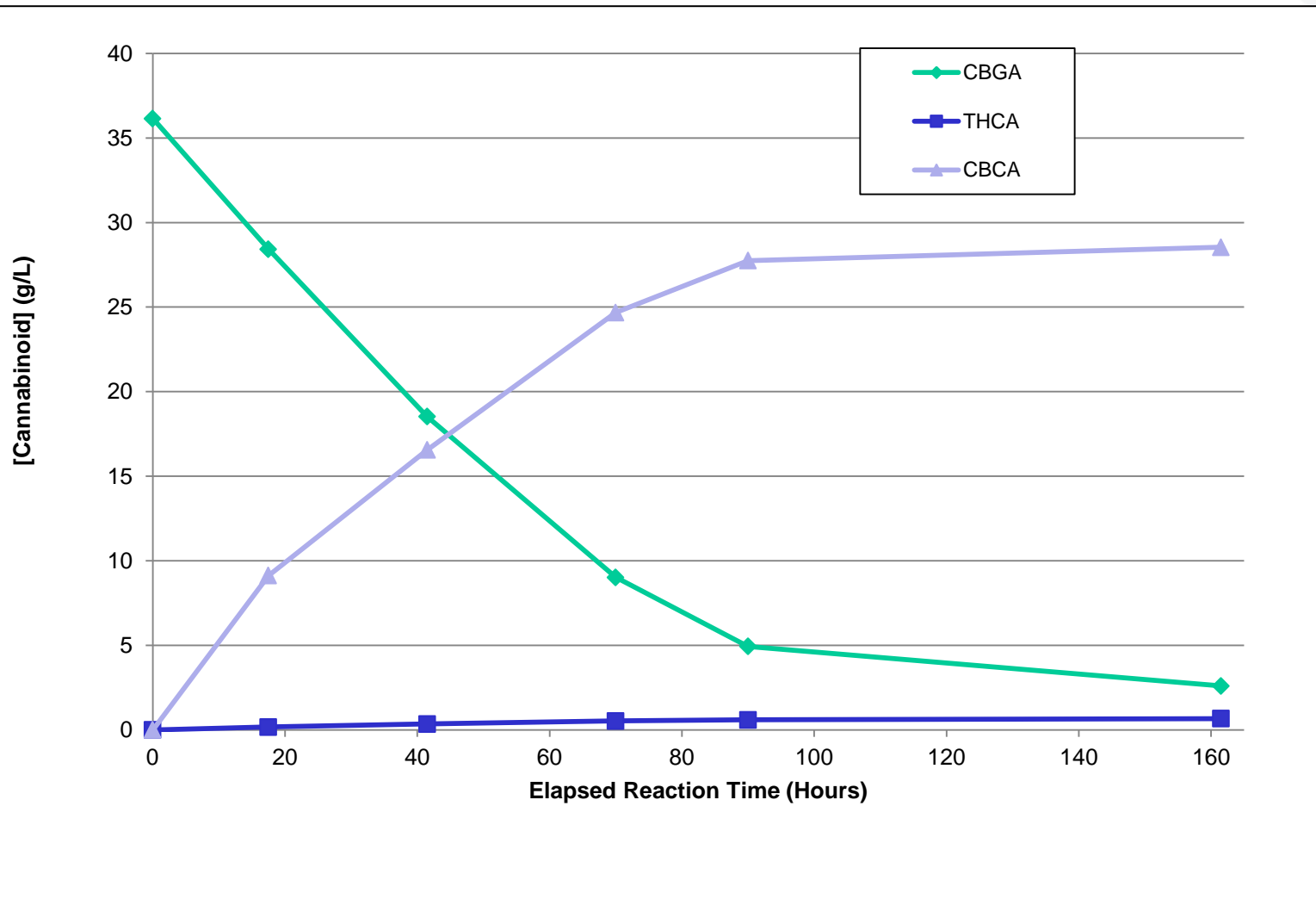
CBGA or CBGVA

- Proprietary Process
- Permits Manufacture of Commercial Quantities of CBGA or CBGVA
- Proprietary Purification Methodology - >95% Purity
- Relatively High Yields: >70%

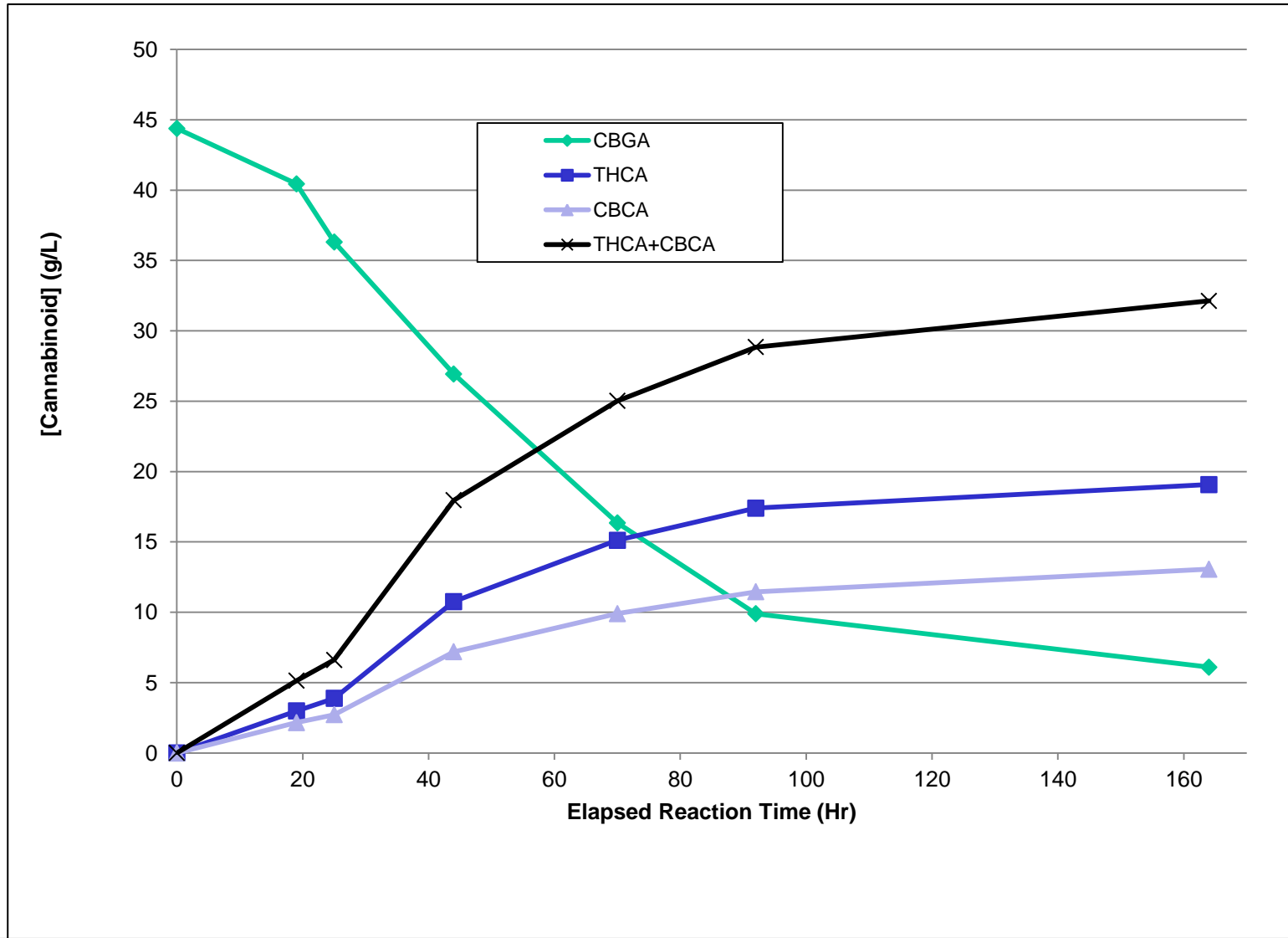
Biocatalytic Production of CBCA

THCA synthase reaction

- ❖ 36 g/L CBGA (substrate)
- ❖ pH optimized for formation of CBCA
- ❖ >95% Conversion of CBGA to cannabinoid products
- ❖ Rapid reaction – about 160 h
- ❖ High Volumetric Efficiency:
~30 g/L
- ❖ CBCA Yield: 29 g/L
- ❖ THCA Yield: ~2 g/L
- ❖ Excellent Product Ratio CBCA:THCA
>40:1



Biocatalytic Production of THCA

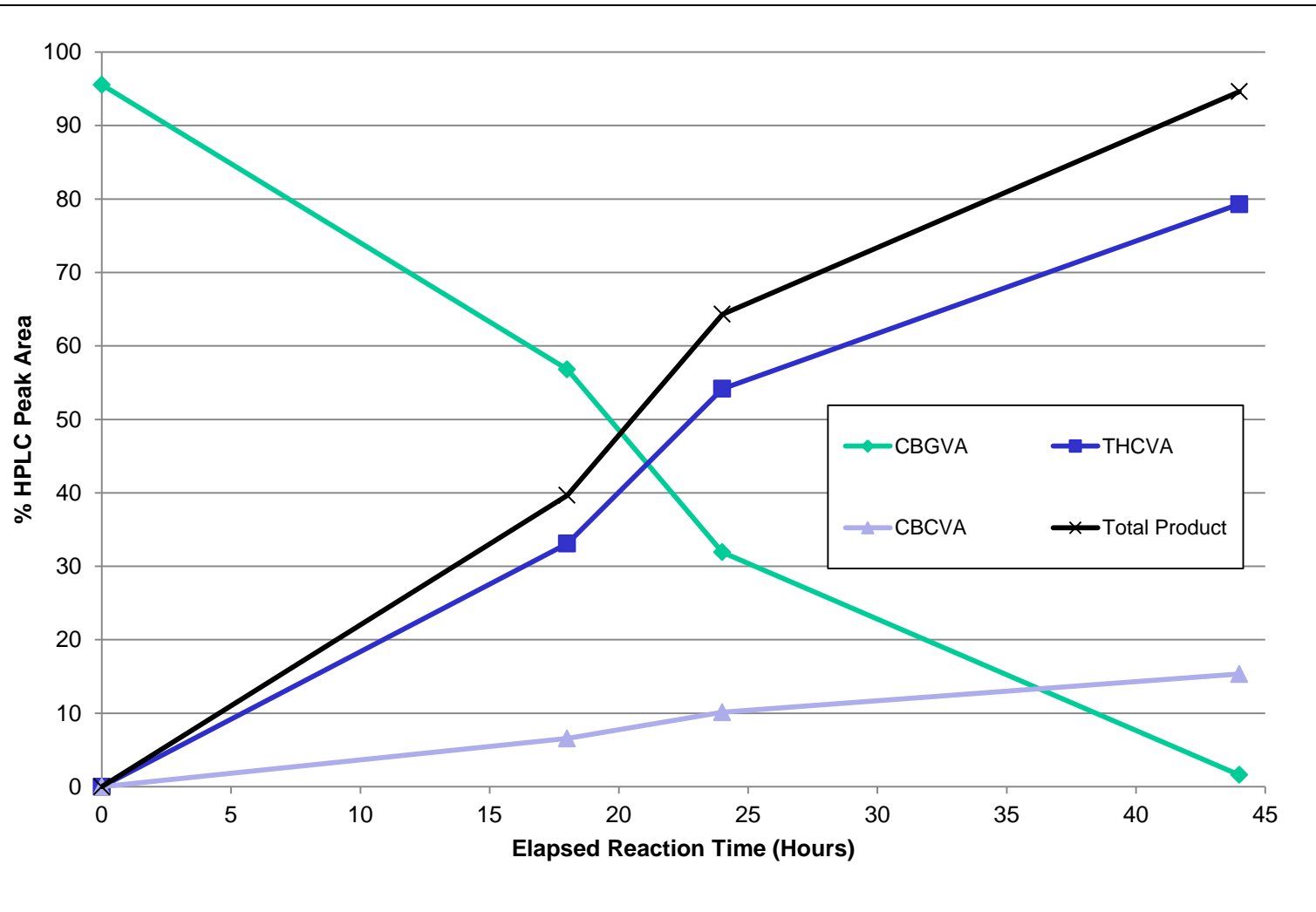


THCA synthase reaction

- ❖ 44 g/L CBGA (substrate)
- ❖ pH optimized for production of THCA
- ❖ >90% Conversion of CBGA to cannabinoid products
- ❖ Rapid reaction – about 160 h
- ❖ High Volumetric Efficiency:
>30 g/L of Total Cannabinoid Products
- ❖ THCA Yield: 19 g/L
- ❖ CBCA Yield: 13 g/L

Biocatalytic Production of Varins

I. Production of THCVA

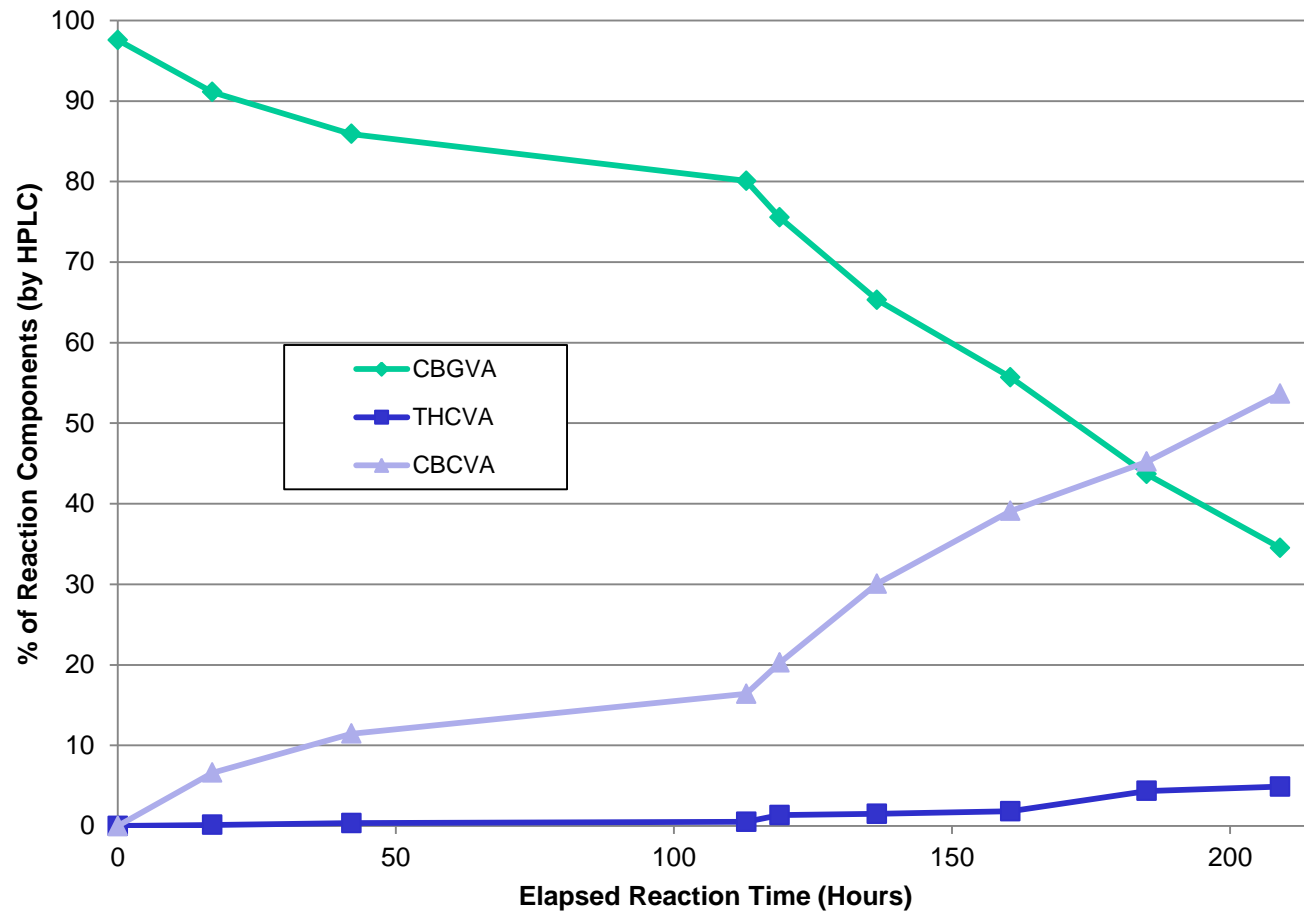


THCA synthase reaction

- ❖ 30 g/L CBGVA (substrate)
- ❖ pH optimized for production of THCVA
- ❖ Rapid reaction – about 45 h
- ❖ >95% Conversion of CBGA to cannabinoid products
- ❖ Good THCVA to CBCVA product ratio
- ❖ THCVA Yield: 24 g/L
- ❖ CBCVA Yield: 5 g/L

Biocatalytic Production of Varins

II. Production of CBCVA

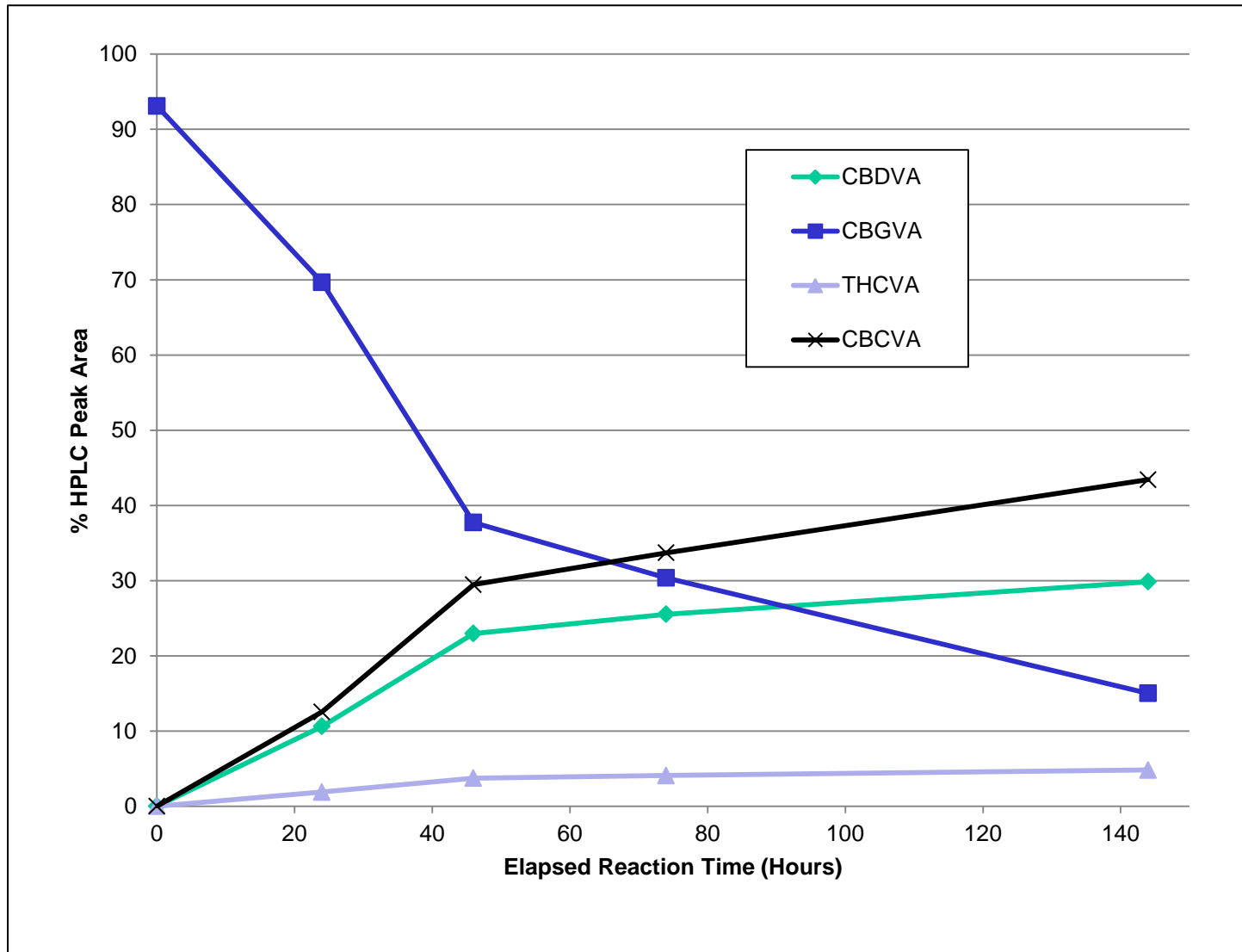


THCA synthase reaction

- ❖ 20 g/L CBGVA (substrate)
- ❖ pH optimized for production of CBCVA
- ❖ Slower reaction than THCA synthase – about 200 h for ~70% Conversion of CBGA to cannabinoid products
- ❖ Reaction not fully optimized
- ❖ CBCVA Yield: 11 g/L
- ❖ THCVA Yield: 2 g/L
- ❖ Good product ratio – CBCVA : THCVA

Biocatalytic Production of Varins

III. Production of CBDVA

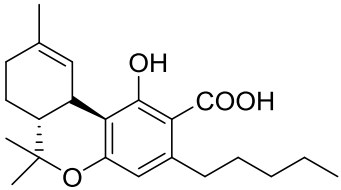


CBDA synthase reaction

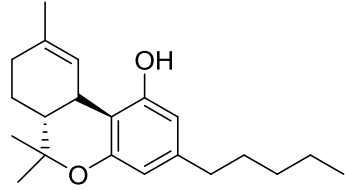
- ❖ 21 g/L CBGVA (substrate)
- ❖ Slower reaction – not as efficient as the reaction for bio-catalytic formation of THCVA
- ❖ Reaction not fully optimized
- ❖ CBCVA Yield: ~10 g/L
- ❖ CBDVA Yield: ~7 g/L
- ❖ THCVA Yield: ~1 g/L
- ❖ Product ratio – Favors CBCVA over CBDVA and THCVA

Cannabinoids Manufactured by CannSynthesis™

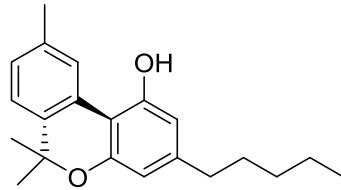
Cannabinoid Compounds



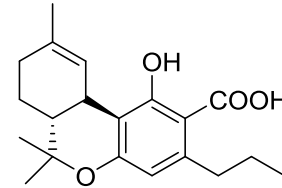
THCA



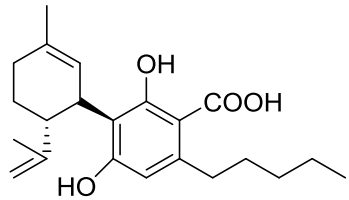
THC



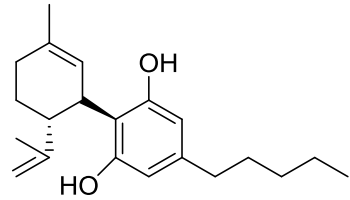
CBN



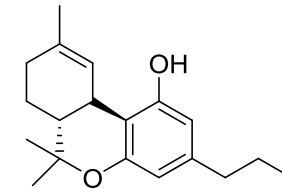
THCVA



CBDA

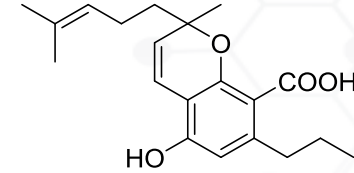


CBD

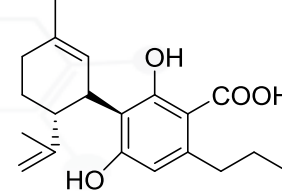


THCV

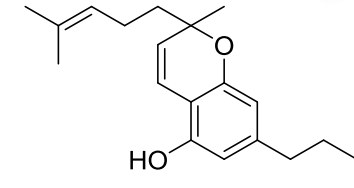
Varin Compounds



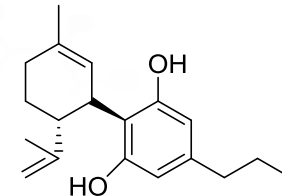
CBCVA



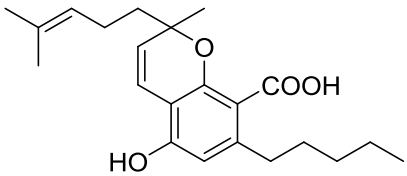
CBDVA



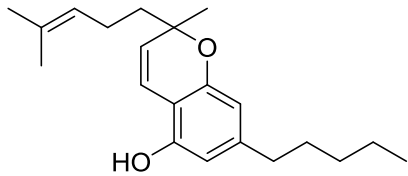
CBCV



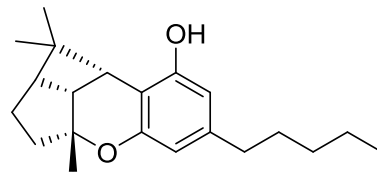
CBDV



CBCA

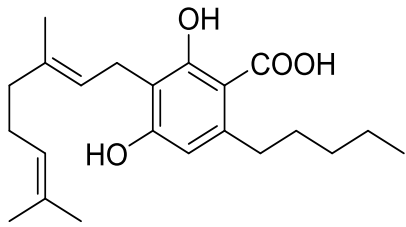


CBC

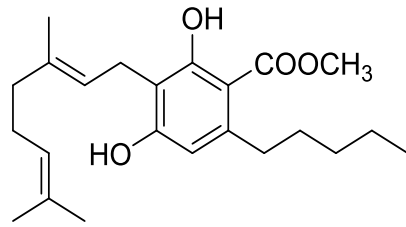


CBL

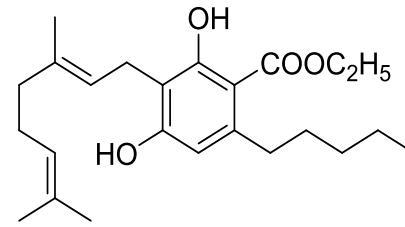
Cannabinoids Manufactured by Teewinot -Cont'd



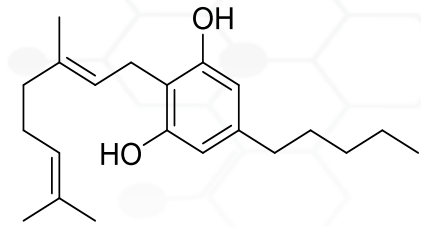
CBGA



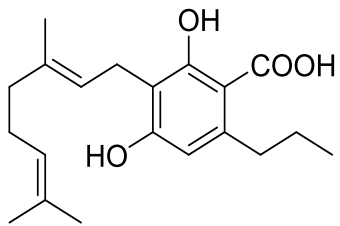
CBGA methyl ester



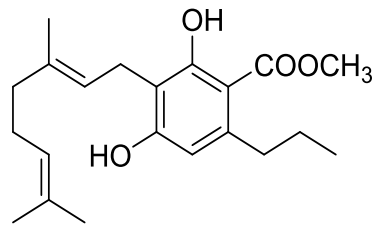
CBGA ethyl ester



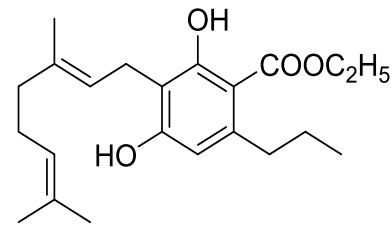
CBG



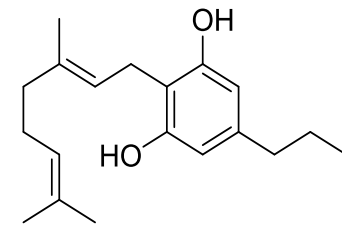
CBGVA



CBGVA methyl ester



CBGVA ethyl ester



CBGV

Confidential

Teewinot's Commercial Activities

- Sale of Analytical Standards
- Sale of non-GMP Cannabinoids for Preclinical Studies
- Contracts for GMP Production of Cannabinoids
- Consulting and Manufacturing Services for Cannabinoid Prodrugs and Analogs
- Preclinical and Clinical Trials

Cann 10 Conference Exhibit Booth 17

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