METABOLIC PATHWAYS-STOICHIOMETRIES OF ACETONE/ ISOPROPANOL-BUTANOL-ETHANOL FERMENTATIONS

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SUMMARY

The main products of acetone - butanol - ethanol and isopropanol - butanol - ethanol fermentations are acetic acid (AA), butyric acid (BA), acetone (A), isopropanol (I), butanol (B), ethanol (E), acetoin (Ac), CO_2 and H_2. Application of a combination approach to these products formation found that there are 31 total possible cases for five products formation in a culture medium (AA, BA, A, B, E or AA, BA, I, B, E) and 127 total possible cases for seven products formation excluding gases (AA, BA, A, I, B, E, Ac). Metabolic pathways for these products formation as well as their corresponding stoichiometries, based on the separation of the complex biochemical pathways into various individual metabolic units, are described. Fourteen different metabolic units at acidogenic and solventogenic phases are determined. The co-utilization of glucose and organic acids for neutral solvents formation is carefully analysed. Combination analysis of the pathways using glucose and acetic acid as co-substrates gives total possible cases of 1013, the same results for the co-substrates of glucose and butyric acid. The co-utilization of glucose, acetic acid and butyric acid has 14175 total metabolic units. Somes of co-metabolic units and stoichiometries are presented. Biochemical pathways based on the author's stoichiometries for experimental data from various researchers are determined and presented.

1. INTITODUCTION

The metabolic pathways of products formation in acetone-butanol-ethanol (ABE) and isopropanol-butanol-ethanol (IBE) fermentations are complicated. To understand the nature of them, various fundamental of the fermentations have been worked out, among these are :

(1) Proposing metabolic pathways (e.g. Rao and Matharasan 1989 ; Linden 1988 ; Awang et al 1988 ; Reardon et al 1987 ; Jones and Woods 1986 ; Ennis et al 1986 ; McNeil and Kristiansen 1986 ; Hagstrom 1985 ; Roger 1984 ; Zeikus 1980 ; Gottschalk 1979 ; Doelle 1975 ; Pimpa and Goma 1983, 1984).

(2) Enzymes characterizations (e.g. Palosaari and Roger 1988 ; Kim and Kim 1988 ; Weisborn et al 1988 ; Yan et al 1988 ; Yu et al 1987 ; Looten et al 1987 ; Roger and Palosaari 1987 ; Durre et al 1987 ; Hiu and Chen 1986 ; Ballongue et al 1986 ; Hutkins and Kashket 1986 ; Aldersh et al 1983).

(3) Product inhibition studies (e.g. Ballongue et al 1987 ; Soucaille et al 1987 ; Pirnpa et al 1982 ; Pimpa 1982 ; Leung and Wang 1981 ; Moreira et al 1981 ; Costa 1981).

(4) The roles of organic acids (e.g. Junnelles et al 1989 ; Rao and Matharasan 1989 ; Huesemann and Papoutsakis 1986 ; Meyer et al 1986 ; Jowell et al 1986 ; Fond et al 1985 ; Hartmanis et al 1984 ; Monot et al 1984 ; Martin et al 1983 ; Pimpa 1982 ; Gottschal. and Morris 1981).

(5) Culture conditioning (e.g. Barbeau et al 1988 ; Welsh et al 1987 ; Yerushalmi and Volesky 1987 ; Fick and Engasser 1986 ; Reyes-Teodoro and Mickelson 1945).

(6) Mutagenesis (e.g. Janati-idrissi et al 1987 ; Roger and Palosaari 1987 ; Junnelles et al 1987 ; Matta-el-Ammouri et al 1986 ; Hermann et al 1985 ; Largier et al 1985 ; Lemmel 1985).

(7) Culture collections (e.g. Pimpa and @Phacharoen 1988a ; Adler et al 1987 ; Calam 1980).

(8) Improvement of strains via genetic engineering (e.g. Oultram et al 1988 ; Oultram and Young 1985 ; Perez-Martinez et at 1968 ; Reysset et at 1988, 1987 ; Youngleson et al 1988 ; Truffaut and Sebald 1988 ; Zappe et al 1987, 1986 ; Reilly and Roger 1987 ; Yu and Pearce 1986 ; Usdin et al 1986 ; Jones et al 1985 ; Luczak et al 1985 ; Lin and Blashek 1984).

(9) Stoichiometries and kinetics (e.g. Yerushalmi et al 1989, 1988, 1986a, 1986b, 1983 ; Ozilgen 1988 ; Qureshi et al 1988 ; Qureshi and Maddox 1988 ; Roffler et al 1987 ; Eckert and Schugerl 1987 ; Reardon et al 1987 ; Votruba et al 1986 ; Fond et al 1986 ; Papoutsakis 1984 ;
Leung 1982 ; Pimpa 1991, 1987, 1986, 1985 ; Pimpa and Phacharoen 1988b).

Using stoichiometric approach invented by the author (Pimpa 1991, 1987, 1986 etc) as a tool, possible metabolic pathways for various products formation of ABE/IBE fermentations are analysed and presented in this paper. Metabolic pathways based on the derived stoichiometries for products formation, corresponding to experimental data from various authors, are written to consider a balance of substrate utilized, main products formed, $NADH/NAD^+$ and FdH_2/Fd produced and used. The role of acetate/acetyl-CoA loop in the proposed pathways is emphasized.

2. ANALYSES OF POSSIBLE METABOLIC PATHWAYS AND THEIR STOICHIOMETRIES

2. 1 Conventions

To simplify the metabolic pathways presented in the subsequent sections, it is necessary to use abreviations and symbols, instead of full names and chemical formulae of the compounds involved. Table 1 shows the desired conventions, The major end products of ABE/IBE fermentations are acetic acid, butyric acid, acetone, isopropanol, n-butanol, ethanol, CO_2 and H_2. Other end products such as lactic acid, acetoin, acetaldehyde can be formed in minor amount by some Clostridia or experimental conditions. All possible cases of five products formation (AA, BA, A, B and E) in the culture broth of ABE fermentation are analysed and presented in Table 2. Total possible cases of five products formation (AA, BA, I, B and E) for IBE fermentation are the same as those of ABE fermentation except replaced A by I. Analysis of all possible cases of ABE/IBE fermentations for seven products formation (AA, BA, A, I, B, E and Ac) gives results as shown in Table 3.

Table 1. Name, symbols and chemical formulae of major compounds in ABE/IBE fermentations

Name	Molecular formula	Structural formular	Short formular and symbol
Acetaldehyde	C_2H_4O	CH_3CHO	-
Acetate	$C_2H_3O^-_2$	CH_3COO^-	-
Acetic acid	$C_2H_4O_2$	CH_3COOH	AA
Acetoacetate	$C_4H_5O_3$	$CH_3COCH_2COO^-$	-
Acetoacetyl-Coenzyme A	-	CH_3COOH_2CO-CoA	Acetoacetyl-CoA
Acetoin	$C_4H_8O_2$	$CH_3CHOHCOCH_3$	Ac
Acetolactate	$C_5H_7O_4$	$CH_3COCH_2CHOHCOO$-	-
Acetone	C_3H_6O	CH_3COCH_3	A
Acetyl-Coenzyme A	-	CH_3CO-CoA	Acetyl-CoA
Acetyl-phosphate	-	$CH_3CO\text{-}OPO^{2-}$	Acetyl-P
n-Butanol	$C_4H_{10}O$	$CH_3CH_2CH_2CH_2OH$	Butanol, B
Butyraldehyde	C_4H_8O	$CH_3CH_2CH_2CHO$	-
Butyrate	$C_4H_7O^-_2$	$CH_3CH_2CH_2COO^-$	-
Butyric acid	$C_4H_8O_2$	$CH_3CH_2CH_2COOH$	Ba
Butyryl-coenzyme A	-	$CH_3CH_2CH_2CO$-CoA	Butyryl-CoA
Butyryl- phosphate	-	$CH_3CH_2CH_2CO\text{-}OPO^{2-}_3$	Butyryl-P
Crotonyl- coenzyme A	-	$CH_3CH\text{-}CHCO$-CoA	Crotonyl-CoA
Diacetyl	$C_4H_6O_2$	$CH_3COCOCH_3$	-
Ethanol	C_2H_6O	CH_3CH_2OH	E
Glucose	$C_6H_{12}O_6$	-	G
3-Hydroxy-butyryl-coenzyme A	-	$CH_3CHOHCH_2CO$-CoA	3-Hydroxy-butyryl-CoA
Isopropanol	C_3H_8O	$CH_3CHOHCH_3$	I
Lactate	$C_3H_5O^-_3$	$CH_3CHOHCOOH$	LA
Pyruvate	$C_3H_3O_3$	CH_3COCOO^-	-
Pyruvic acid	$C_3H_4O_3$	$CH_3COCOOH$	Py

Table2. All possible cases of five products formation from glucose for ABE. Fermentation

Total and Products Formed in medium	Amounts of Possible cases	Case number	End products formed	Gas produced
1	5	1	AA	CO_2 and H_2
		2	BA	CO_2 and H_2
		3	A	CO_2 and H_2
		4	B	CO_2
		5	E	CO_2
2	10	1	AA and BA	CO_2 and H_2
		2	AA and A	CO_2 and H_2
		3	AA and B	CO_2 and H_2
		4	AA and E	CO_2 and H_2
		5	BA and A	CO_2 and H_2
		6	BA and B	CO_2 and H_2
		7	BA and E	CO_2 and H_2
		8	A and B	CO_2 and H_2
		9	A and E	CO_2 and H_2
		10	B and E	CO_2
3	10	1	AA, BA and A	CO_2 and H_2
		2	AA, BA and B	CO_2 and H_2
		3	AA, BA and E	CO_2 and H_2
		4	AA, A and B	CO_2 and H_2
		5	AA, A and E	CO_2 and H_2
		6	AA, B and E	CO_2 and H_2
		7	BA, A and B	CO_2 and H_2
		8	BA, A and E	CO_2 and H_2
		9	BA, B and E	CO_2 and H_2
		10	A,B and E	CO_2 and H_2
4	5	1	AA, BA, A and B	CO_2 and H_2
		2	AA, BA, A and E	CO_2 and H_2
		3	AA, BA, B and E AA,	CO_2 and H_2
		4	A, B and E	CO_2 and H_2
		5	BA, A, B and E	CO_2 and H_2
5	1	1	AA, BA, A, B and E	CO_2 and H_2

Table 3. All possible cases of seven products formation (AA, BA, A, I, B, E and Ac) from Glucose in a culture medium for ABE/IBE fermentations

Total and Products Formed in medium	Possible cases	Case number	End products formed	Gas produced
1	7	1	AA	CO_2 and H_2
		2	BA	CO_2 and H_2
		3	A	CO_2 and H_2
		4	I	CO_2 and H_2
		5	B	CO_2
		6	E	CO_2
		7	Ac	CO_2 and H_2
2	21	1	AA and BA	CO_2 and H_2
		2	AA and A	CO_2 and H_2
		3	AA and I	CO_2 and H_2
		4	AA and B	CO_2 and H_2
		5	AA and E	CO_2 and H_2
		6	AA and Ac	CO_2 and H_2
		7	BA and A	CO_2 and H_2
		8	BA and I	CO_2 and H_2
		9	BA and B	CO_2 and H_2
		10	BA and E	CO_2 and H_2
		11	BA and Ac	CO_2 and H_2
		12	A and I	CO_2 and H_2
		13	A and B	CO_2 and H_2
		14	A and E	CO_2 and H_2
		15	A and Ac	CO_2 and H_2
		16	I and B	CO_2 and H_2
		17	I and E	CO_2 and H_2
		18	I and Ac	CO_2 and H_2
		19	B and B	CO_2 and H_2
		20	B and Ac	CO_2 and H_2
		21	E and Ac	CO_2 and H_2

Total and Products Formed in medium	Possible cases	Case number	End products formed	Gas produced
3	35	1	AA, BA and A	CO_2 and H_2
		2	AA, BA and I	CO_2 and H_2
		3	AA, BA and B	CO_2 and H_2
		4	AA, BA and E	CO_2 and H_2
		5	AA, BA and Ac	CO_2 and H_2
		6	AA, A and I	CO_2 and H_2
		7	AA, A and B	CO_2 and H_2
		8	AA, A and E	CO_2 and H_2
		9	AA, A and Ac	CO_2 and H_2
		10	AA, I and B	CO_2 and H_2
		11	AA, I and E	CO_2 and H_2
		12	AA, I and Ac	CO_2 and H_2
		13	AA, B and E	CO_2 and H_2
		14	AA, B and Ac	CO_2 and H_2
		15	AA, E and Ac	CO_2 and H_2
		16	BA, A and I	CO_2 and H_2
		17	BA, A and B	CO_2 and H_2
		18	BA, A and E	CO_2 and H_2
		19	BA, A and Ac	CO_2 and H_2
		20	BA, I and B	CO_2 and H_2
		21	BA, I and E	CO_2 and H_2
		22	BA, I and Ac	CO_2 and H_2
		23	BA, B and E	CO_2 and H_2
		24	BA, B and Ac	CO_2 and H_2
		25	BA, E and Ac	CO_2 and H_2
		26	A, I and B	CO_2 and H_2
		27	A, I and E	CO_2 and H_2
		28	A, I and Ac	CO_2 and H_2
		29	A, B and E	CO_2 and H_2
		30	A, B and Ac	CO_2 and H_2
		31	A, E and Ac	CO_2 and H_2
		32	I, B and E	CO_2 and H_2
		33	I, B and Ac	CO_2 and H_2
		34	I, E and Ac	CO_2 and H_2
		35	B, E and Ac	CO_2 and H_2

Total and Products Formed in medium	Possible cases	Case number	End products formed	Gas produced
4	35	10	AA, BA, E and Ac	CO_2 and H_2
		11	AA, A, I and B	CO_2 and H_2
		12	AA, A, I and E	CO_2 and H_2
		13	AA, A,I and Ac	CO_2 and H_2
		14	AA, A, B and E	CO_2 and H_2
		15	AA, A, B and Ac	CO_2 and H_2
		16	AA, A, E and Ac	CO_2 and H_2
		17	AA, I, B and E	CO_2 and H_2
		18	AA, I, B and Ac	CO_2 and H_2
		19	AA, I, E and Ac	CO_2 and H_2
		20	AA, B, E and Ac	CO_2 and H_2
		21	BA, A, I and B	CO_2 and H_2
		22	BA, A, I and E	CO_2 and H_2
		23	BA, A, I and Ac	CO_2 and H_2
		24	BA, A, B and E	CO_2 and H_2
		25	BA, A, B and Ac	CO_2 and H_2
		26	BA, A, E and Ac	CO_2 and H_2
		27	BA, I, B and E	CO_2 and H_2
		28	BA, I, B and Ac	CO_2 and H_2
		29	BA, I, E and Ac	CO_2 and H_2
		30	BA, B, E and Ac	CO_2 and H_2
		31	A, I, B and E	CO_2 and H_2
		32	A, I, B and Ac	CO_2 and H_2
		33	A, I, E and Ac	CO_2 and H_2
		34	A, B, E and Ac	CO_2 and H_2
		35	I, B, E and Ac	CO_2 and H_2
5	21	1	AA, BA, A, I and B	CO_2 and H_2
		2	AA, BA, A, I and E	CO_2 and H_2
		3	AA, BA, A, I and Ac	CO_2 and H_2
		4	AA, BA, A, B and E	CO_2 and H_2
		5	AA, BA, A, B and Ac	CO_2 and H_2
		6	AA, BA, A, E and Ac	CO_2 and H_2
		7	AA, BA, I, B and E	CO_2 and H_2
		8	AA, BA, I, B and Ac	CO_2 and H_2

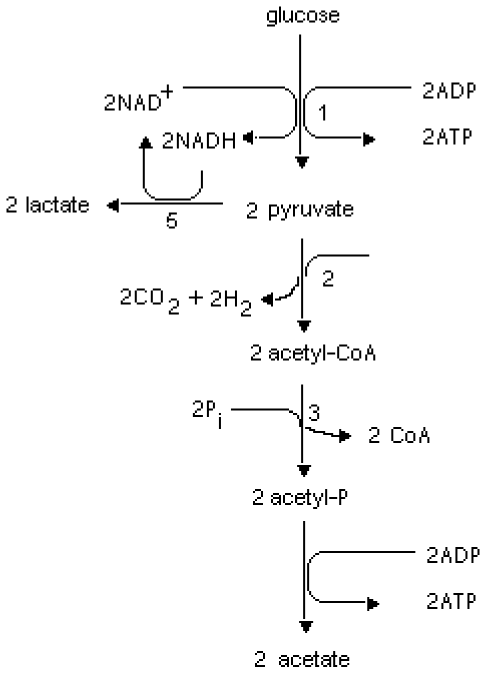
Total and Products Formed in medium	Possible cases	Case number	End products formed	Gas produced
		9	AA, BA, I, E and Ac	CO_2 and H_2
		10	AA, BA, B, E and Ac	CO_2 and H_2
		11	AA, A, I, B and E	CO_2 and H_2
		12	AA, A, I, B and Ac	CO_2 and H_2
		13	AA, A, I, E and Ac	CO_2 and H_2
		14	AA, A, B, E and Ac	CO_2 and H_2
		15	AA, I, B, E and Ac	CO_2 and H_2
		16	BA, A, I, B and E	CO_2 and H_2
		17	BA, A, I, B and Ac	CO_2 and H_2
		18	BA, A, I, E and Ac	CO_2 and H_2
		19	BA, A, B, E and Ac	CO_2 and H_2
		20	BA, I, B, E and Ac	CO_2 and H_2
6	7	21	A, I, B, E and Ac	CO_2 and H_2
		1	AA, BA, A, I, B and E	CO_2 and H_2
		2	AA, BA, A, I, B and Ac	CO_2 and H_2
		3	AA, BA, A, I, E and Ac	CO_2 and H_2
		4	AA, BA, A, B, E and Ac	CO_2 and H_2
		5	AA, BA, I, B, E and Ac	CO_2 and H_2
		6	AA, A, I, B, E and Ac	CO_2 and H_2
		7	BA, A, I, B, E and Ac	CO_2 and H_2
7	1	1	AA, BA, A, I, B, E and Ac	CO_2 and H_2

2.2 Proposed Metabolic Pathways and Their Stoichiometries

Separation of the complex biochemical pathways of ABE/IBE fermentations into various different individual metabolic units corresponding to products formation is the approach for proposing biochemical pathways-stoichiometries presented in the subsequent sections. Metabolic units for acidogenesis are firstly derived, followed by those for solventogenesis

2.2.1 Units of Metabolic Pathways at Acidogenesis

There are two metabolic units in the stage of organic acids formation. The first one is the unit of acetic and lactic acids formation from carbohydrate, as glucose (Fig. 1). The second unit is the metabolic unit of butyric acid formation from glucose (Fig. 2).



Stoichiometry : $G + 2H_2O \rightarrow 2AA + 2CO_2 + 4H_2$

$G \rightarrow 2LA$

Figure 1 Metabolic unit of acetic acid (AA) and lactic acid (LA) production from glucose (G) by butyric acid bacteria fermentations. The pathways or enzyme systems for the reactions shown are as follows : (1) the Embden-Meyerhof-Parnas pathways ; (2) pyruvate-ferredoxin oxidoreductase, hydrogenase, NADH-ferredoxin oxidoreductase, NADPH-ferredoxin oxidoreductase ; (3) phosphotransacetylase (phosphate acetyl-transferase or phosphate transacylase) ; (4) acetate kinase ; (5) lactate dehydrogenase.

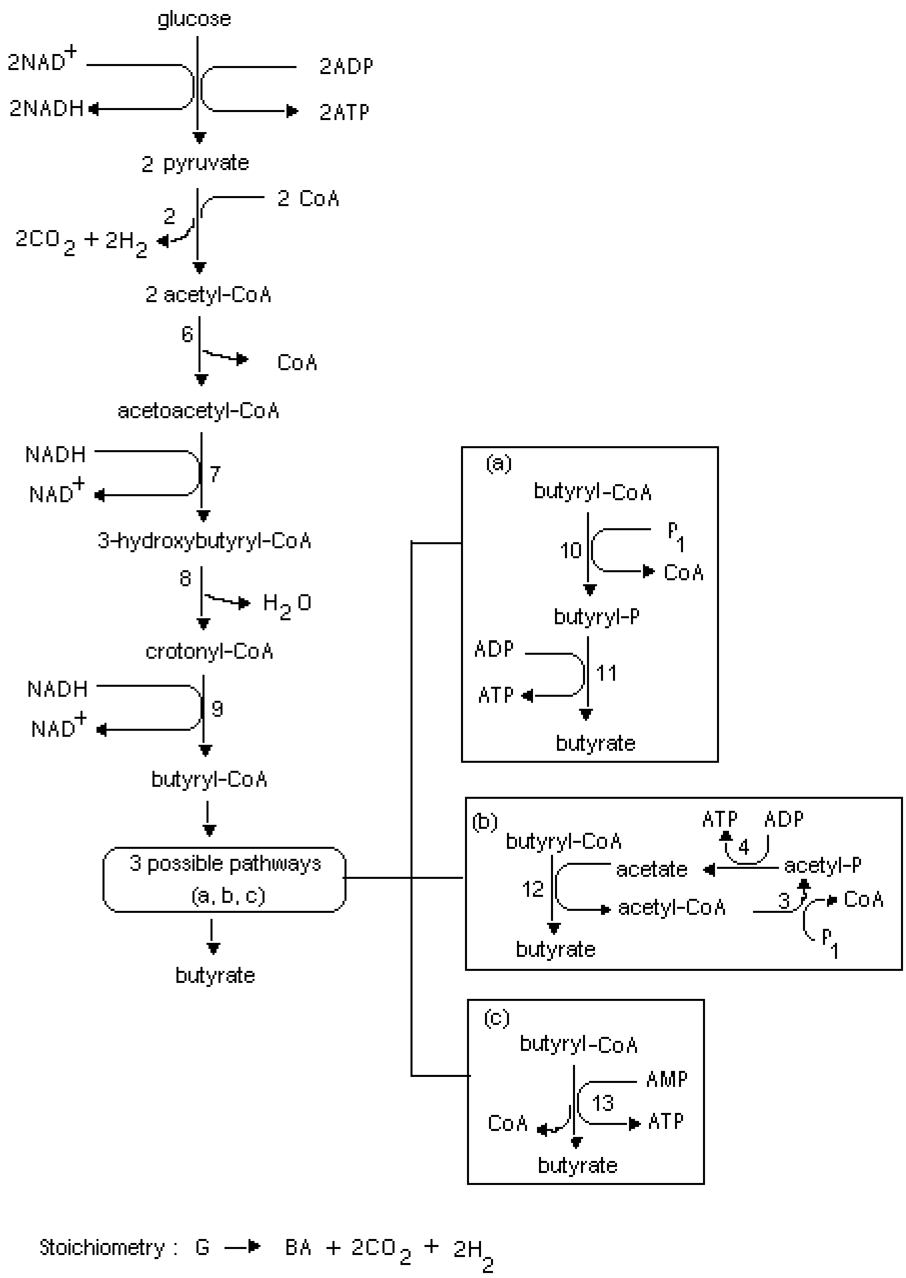


Figure 2 Metabolic unit of butyric acid (BA) production from glucose (G) at acidogenic stage. The enzyme systems for the reactions shown are as follows : (6) thiolase (acetyl-CoA acetyltransferase) ; (7) 3- hydroxybutyryl-CoA dehydrogenase ; (8) crotonase ; (9) butyryl-CoA dehydrogenase ; (10) phosphate butyltransferase (phosphotrans-butylase) ; (11) butyrate kinase ; (12) CoA transferase ; (13) butyryl-CoA/butyrate thiokinase.

The unit of acetic acid formation produces an energy-rich compound (4 moles of ATP per mole of glucose utilized or 2 moles of ATP per mole of acetic acid produced) and a reducing agent (2 moles of NADH per mole of glucose utilized) which are necessary for synthetic and other activities concerned. The excess produced NADH is converted to H_2 via FdH_2 formation by the aid of NADH-ferridoxin oxidoreductase and hydrogenase (Fig. 3). The values of H_2 produced from NADH at various experimental conditions of ABE/IBE fermentations are quantitatively presented in Section 3 (Figs. 15, 20.II and 23.I). Stoichiometric equations for acetic acid formation from glucose (Eqs. I to 5) and lactic acid formation (Eqs. 6 to 8) are derived in details. In the subsequent sections, only the simple forms are mentioned.

$$G + 4ADP + 4P + 2NAD^+ \longrightarrow 2\text{ acetate} + 4ATP + 2NADH + 2H^+ + 2CO_2 + 2H_2 \quad (1)$$

$$G + 2NAD^+ \longrightarrow 2\text{ acetate} + 2NADH + 2H^+ + 2CO_2 + 2H_2 \quad (2)$$

$$G + 2H_2O \longrightarrow 2\text{ acetate} + 2H^+ + 2CO_2 + 4H_2 \quad (3)$$

$$G + 2H_2O \longrightarrow 2\text{ acetic acid} + 2CO_2 + 4H_2 \quad (4)$$

$$G + 2H_2O \longrightarrow 2AA + 2CO_2 + 4H_2 \quad (5)$$

$$G + 2ADP + 2P_i \longrightarrow 2\text{ lactate} + 2H^+ + 2ATP \quad (6)$$

$$G \longrightarrow 2\text{ lactate} + 2H^+ \quad (7)$$

$$G \longrightarrow 2LA \quad (8)$$

Acidic environment caused by the accumulation of acetic acid in the culture medium encounters the microorganism to find out a pathway to solve it. The metabolic unit of glucose conversion to butyric acid as shown in Fig. 2 can serve this purpose, accumulated acetic acid is converted to acetyl-CoA by CoA transferase. The unit has two other alternative pathways for conversion of butyryl-CoA to butyrate, without acetate/acetyl-CoA loop as coenzymes. NADH produced by EMP system is used up within the unit. Excess NADH formed from the metabolic unit of glucose conversion to acetic acid can be used by the new unit. Three moles of ATP produced per mole of glucose utilized or butyric acid formed. A simple stoichiometry for butyric acid formation from glucose is Eq. 9.

$$G \longrightarrow BA + 2CO_2 + 2H_2 \quad (9)$$

At the end of acidogenesis, the net excess NADH is converted to H_2 via FdH_2 formation (Fig. 3). The metabolic unit of butyric acid formation from glucose creates a new acidic environment, caused by accumulated butyric acid. However the unit can eliminate some accumulated acetic acid, eventhough not all.

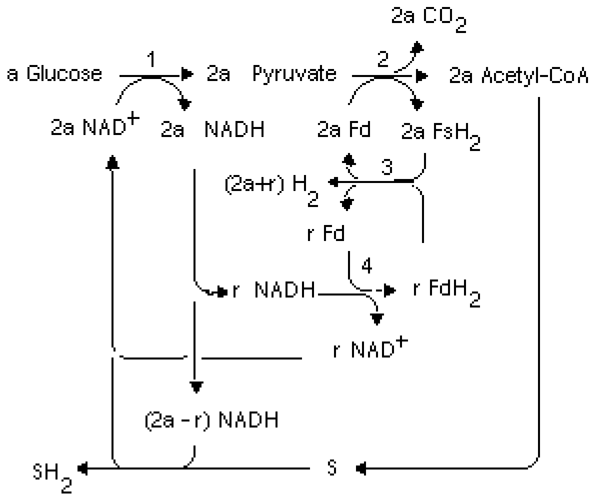


Figure 3 Metabolic scheme and balances of reducing agents formed and used at acidogenesis for butanol fermentations. Symbols, enzymes and enzyme systems used are as follows : (1) Enzyme systems of Embden-Meyerhof-Parnas (EMP) Pathways ; (2) Pyruvate-ferredoxin oxidoreductase ; (3) Hydrogenase ; (4) NADH-ferredoxin oxidoreductase, S = Oxidised forms of intermediates and/or products, SH_2 Reduced forms of intermediates and/or products, Fd = Oxidised form of ferredoxin, FdH_2 = Reduced form of ferredoxin, a = moles of glucose (G) or hexose equivalent used for products formation, r = moles of NADH converted to FdH_2 and then to H_2 via enzymes (3) and (4).

2.2.2 Units of Metabolic Pathways at Solventogenesis

Biochemical pathways followed up the acidogenic phase of ABE/IBE fermentations should have the following characteristics : (1) acidic environment can be solved, (2) the accumulated acetic and butyric acids can be used as substrates, co-substrates, coenzymes, enzyme inducers and/or regulators, etc., (3) excess NADH previously produced can be used, instead of conversion to H_2. It is well-known that the main products of ABE/IBE fermentations at solventogenesis are acetone, isopropanol, butanol, ethanol and acetoin. The metabolic pathways for neutral solvents formation, based on substrates used, can be divided into three groups : (1) metabolic units of glucose conversion to solvents, (2) metabolic units of organic acids conversion to solvents, and (3) metabolic units of solvents formation from the co-utilization of glucose and organic acids.

2.2.2.1 Metabolic Units of Glucose Conversion to Solvents

There are 4 metabolic units : (1) acetone/isopropanol formation (Fig. 4), (2) butanol formation (Fig. 5), (3) ethanol formation (Fig. 6), and (4) acetoin formation (Fig. 7) . Simple stoichiometries corresponding to these metabolic units are as follows :

For acetone formation from glucose :

$$G + H_2O \longrightarrow A + 3CO_2 + 4H_2 \qquad (10)$$

For isopropanol formation from glucose :

$$G + H_2O \longrightarrow I + 3CO_2 + 3H_2 \qquad (11)$$

For butanol formation from glucose :

$$G \longrightarrow B + 2CO_2 + 3H_2O \qquad (12)$$

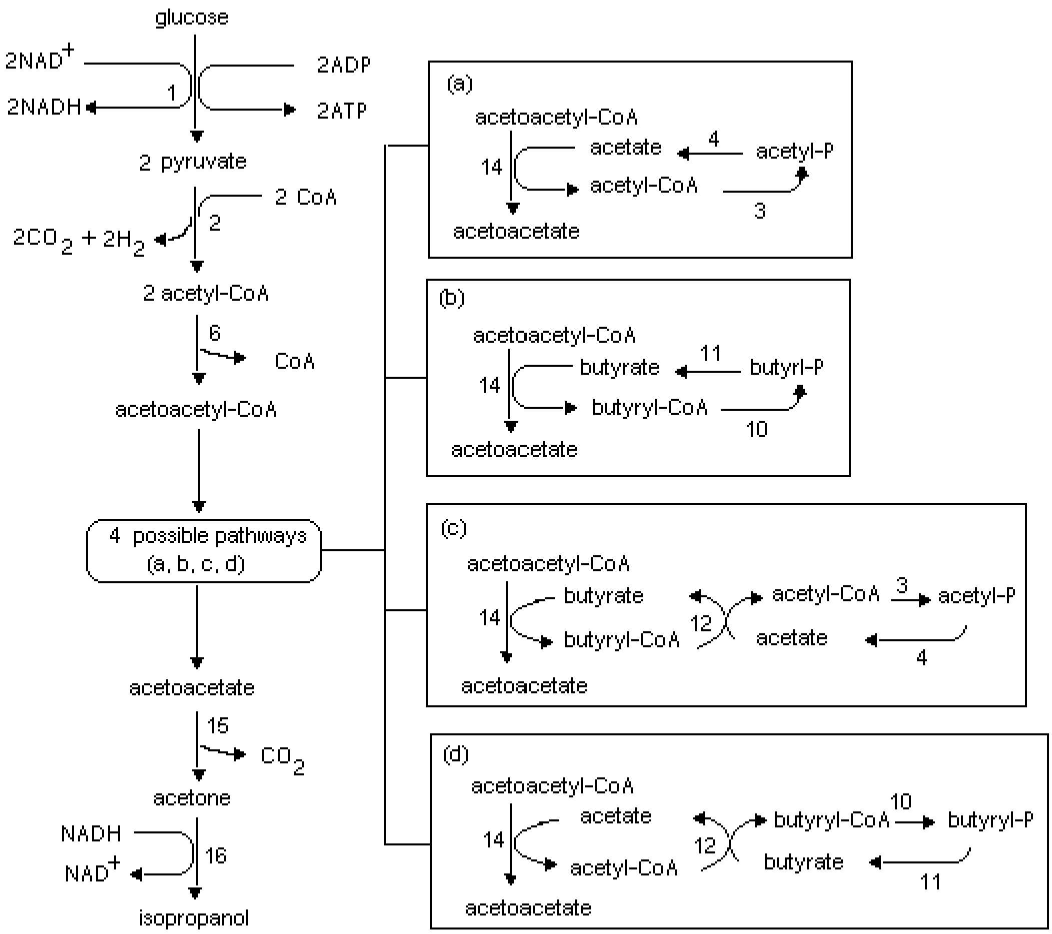
For ethanol formation from glucose :

$$G \longrightarrow 2E + 2CO_2 \qquad (13)$$

For acetoin formation from glucose :

$$G \longrightarrow Ac + 2CO_2 + 2\,H_2 \qquad (14)$$

The metabolic unit of glucose conversion to acetone/isopropanol has the following characteristics excess NADH is produced (for acetone formation, 2 moles of NADH per mole of glucose used ; for isopropanol formation, I mole of NADH per mole of glucose utilized) ; three moles of excess ATP are produced per mole of glucose used ; acetate, butyrate and acetate pIus butyrate act as coenzymes for conversion of acetoacetyl-CoA to acetoacetate. Four different catalytic loops of organic acids for conversion of acetoacetyl-CoA to acetoacetate are proposed : only acetate is involved (Fig. 4a), only butyrate is involved (Fig. 4b) both acetate and butyrate are involved (Fig. 4c and Fig. 4d).



Stoichiometry: $G + H_2O \rightarrow A + 3CO_2 + 4H_2$

$G + H_2O \rightarrow I + 3CO_2 + 3H_2$

Figure 4 Metabolic unit of acetone (A)/isopropanol (I) production from glucose (G) at solventogenic stage. The enzyme systems for the reactions shown are as follows : (14) acetoacetyl-CoA : acetate / butyrate : CoA transferase ; (15) acetoacetate decarboxylase (16) isopropanol dehydrogenase.

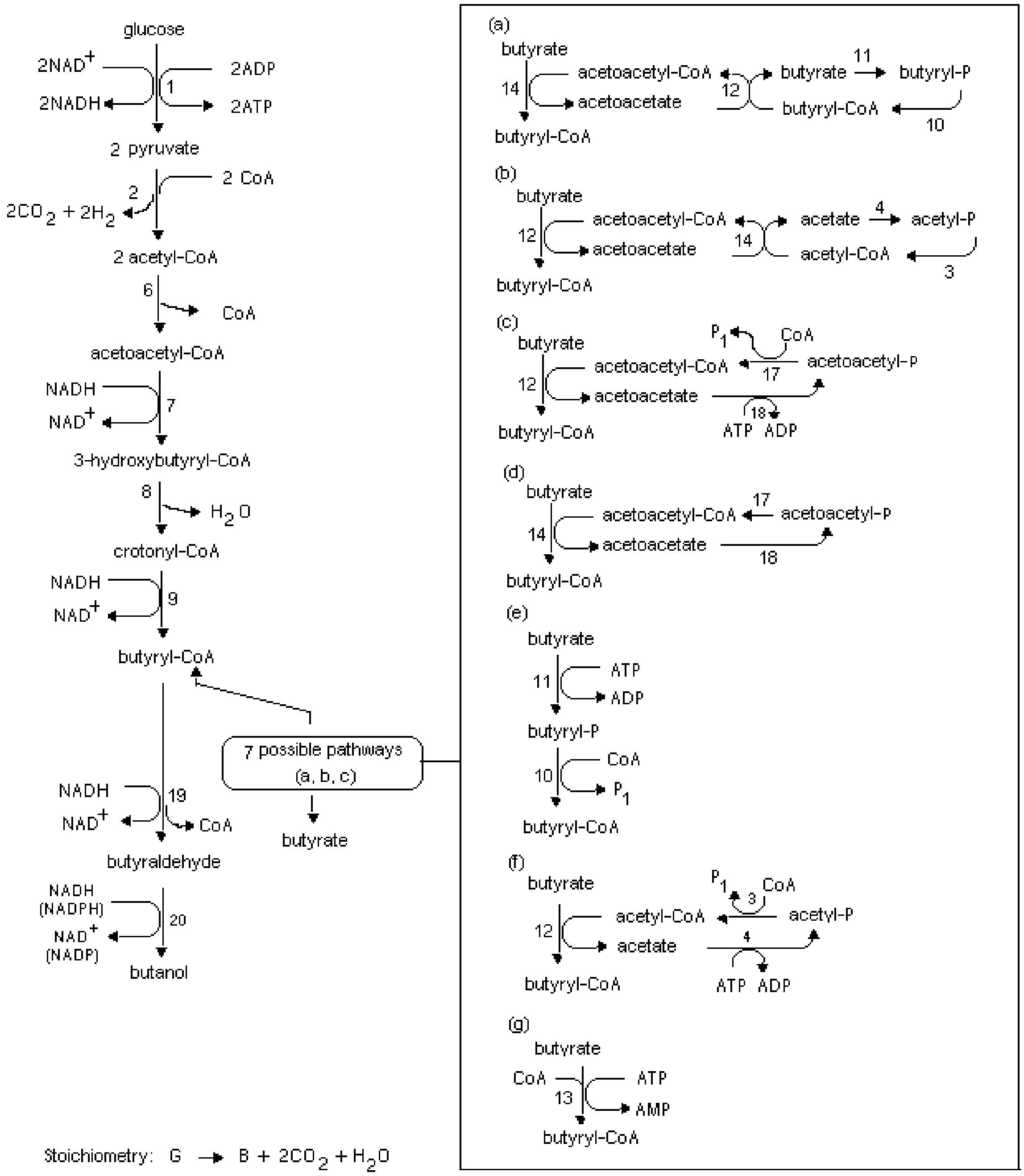


Figure 5 Metabolic unit of butanol (B) production from glucose (G) at solventogenic stage. The enzyme systems for the reactions shown are as follows : (17) phosphotransaceto- acetylase ; (18) acetoacetate kinase ; (19) butyraldehyde dehydrogenase ; (20) butanol dehydrogenase.

The metabolic unit of glucose conversion to butanol (Fig. 5) has the following characteristic : NADH produced via EMP systems is not enough for reduction activity of the unit, NADH must be produced from FdH_2 (Fig. 8) for the synthesis of one mole of butanol from one mole of glucose ; one mole of excess ATP is produced per mole of glucose used ; acetate, acetoacetate, acetoacetate plus acetate and acetoacetate plus butyrate can be used as coenzymes for conversion of accumulated butyrate to butyryl-CoA. Seven different routes for conversion of butyrate to butyryl-CoA are proposed : only acetate system is involved (Fig. 5f), only acetoacetate system is involved (Fig. 5c and Fig. 5d), acetate-acetoacetate system is involved (Fig. 5b), acetoacetate-butyrate system is involved (Fig. 5a) and ATP system is involved (Fig. 5e and Fig. 5g). This metabolic unit allows excess NADH produced via other units (metabolic unit of acetic acid formation from glucose and metabolic unit of acetone / isopropanol formation from glucose) to be utilized. Butanol formation by this unit is rather difficult due to limitation of the reducing agent.

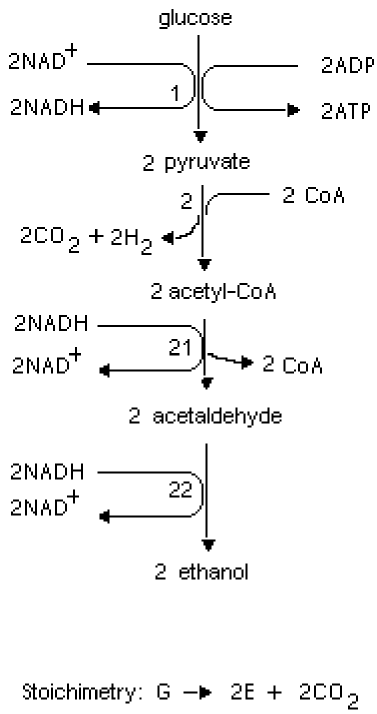


Figure 6 Metabolic unit of ethanol (E) production from glucose (G) at solventogenic stage. The enzyme systems for the reactions shown are as follows : (21) acetaldehyde dehydrogenase ; (22) ethanol dehydrogenase.

The metabolic unit of glucose conversion to ethanol (Fig. 6) has the following characteristics : NADH produced via EMP systems is not enough for reduction of two moles of ethanol from one mole of glucose used, NADH has to be produced from FdH_2 (Fig. 8) ; two moles of excess ATP are produced per mole of glucose utilized ; catalytic role of acetate or butyrate is not involved. This unit can utilize excess NADH produced by other donner units. Limtation of its own produced NADH makes the unit have difficulty.

The metabolic unit of glucose conversion to acetoin (Fig. 7) has the following characteristics : NADH produced by EMP systems is enough for reduction activity of the unit ; two moles of excess ATP are produced per mole of glucose utilized ; acetyl-CoA, acetaldehyde, acetolactate, lactate and diacetyl are intermediates of acetoin formation from pyruvate. Seven different biochemical pathways are proposed. Among these, acetoin formation via acetyl-CoA utilization (Fig. 7c and Fig. 7d) should be preferent, due to available acetyl-CoA formed in the broth of ABE/IBE fermentation. However enzymes of these reactions should be further investigated.

It is important to note that large amounts of NADH are required for solvents production at solventogenic phase. NADH supplied by EMP pathways is not sufficient, NADH produced from FdH_2 (Fig. 8) is necessary. Calculated amounts of these NADH based on experimental data from various authors are shown in Figs. 16, 17, 18, 19, 20.I, 20.III, 20.IV, 20.V, 21, 23.II and 24.

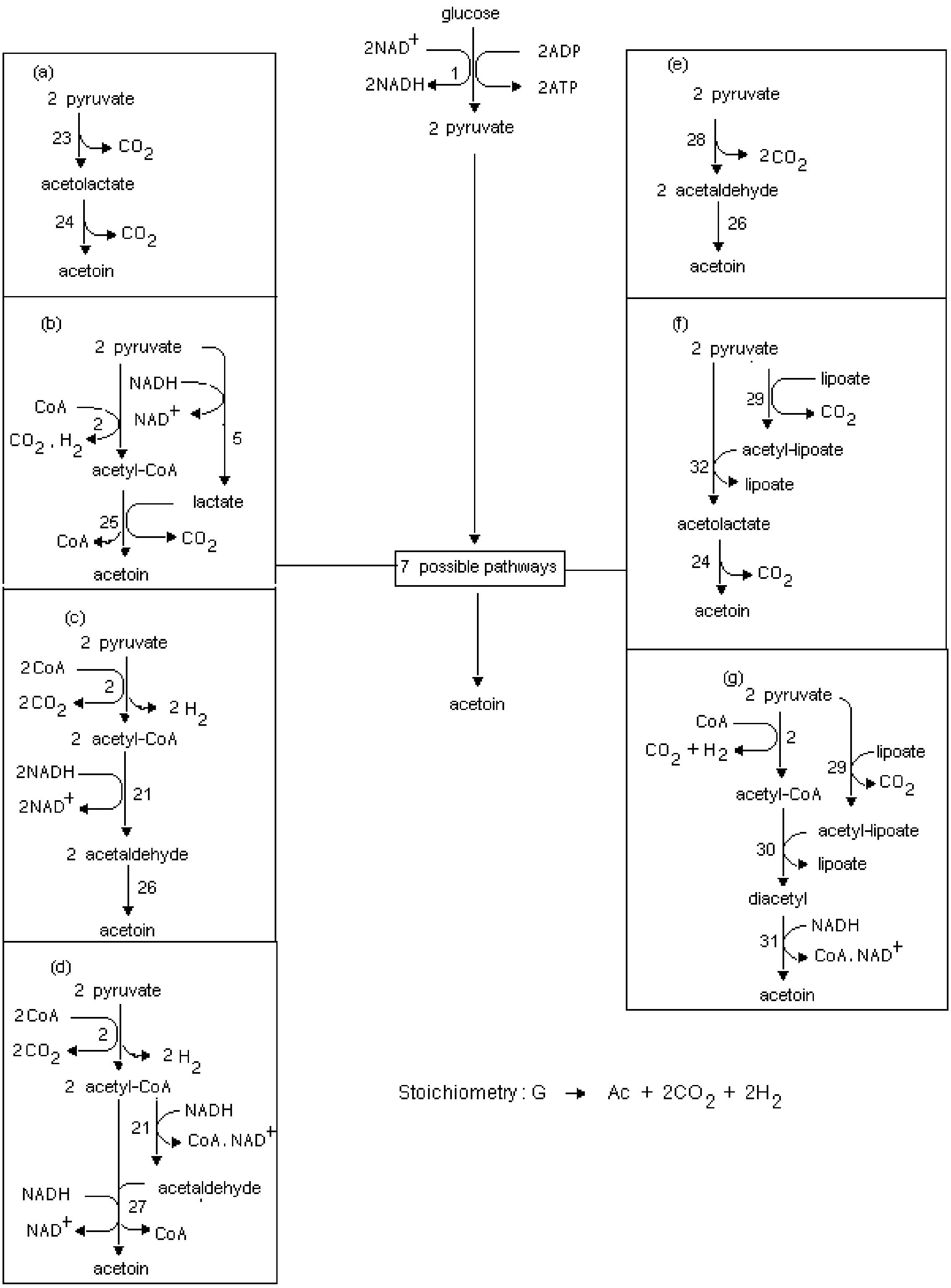


Figure 7 Metabolic unit of acetoin (Ac) formation from glucose (G) at solventogenic stage. The enzyme systems for the reactions shown are as follows : (23) acetolactate synthase (pyruvate/pyruvate) ; (24) acetolactate decarboxylase ; (25) acetoin synthase (acetyl- CoA/lactate) ; (26) acetoin

synthase (acetaldehyde/acetaldehyde) ; (27) acetoin synthase (acetyl-CoA/acetaldehyde) ; (28) pyruvate decarboxylase (pyruvate/acetal- dehyde) ; (29) pyruvatelipoate oxidoreductase ; (30) diacetyl synthase (acetyl-lipoate / acetyl-CoA) ; (31) acetoin dehydrogenase ; (32) acetolactate synthase (pyruvate / acetyl- lipoate).

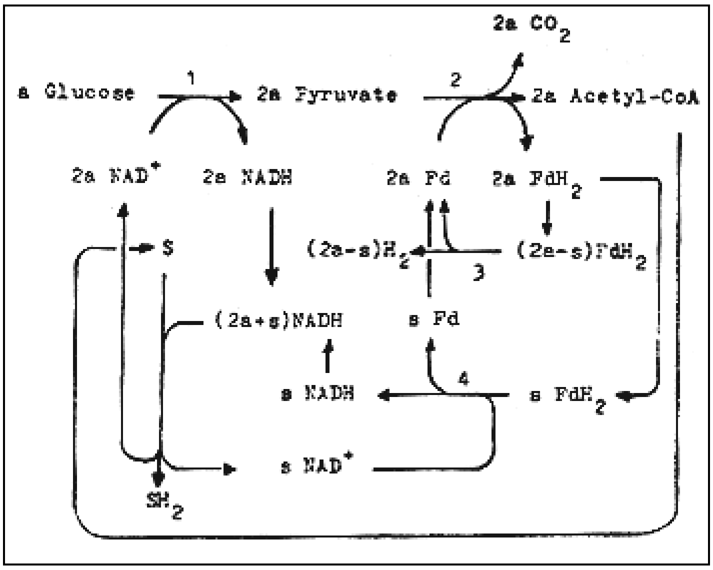


Figure 8 Metabolic scheme and balances of reducing agents at solventogenesis for butanol fermentations. Symbols, enzymes and enzyme systems used are the same as mentioned in Fig. 3, except s is moles of NADH formed from FdH_2

2.2.2.2 Metabolic Units of Solvents Formation from Organic Acids

The main organic acids accumulated in the fermentation broth of ABE/IBE fermentations at the beginning of solventogenesis are acetic and butyric acids. There should be some biochemical pathways for direct conversion of these acids to neutral compounds, using excess NADH produced by other donner metabolic units. Studies with $CH_3C^{13}OOH$ addition, Wood et al 1945 found that the major recovery of C^{13} of added acetic acid was in butanol (55%), CO_2 (18%) and acetone (15%) for **Clostridium acetobutylicum** and was in butanol (43%), CO_2 (26%) and isopropanol (19%) for **Cl. butylicum**. Matta-el-Amouri et al 1985 reported that acetic addition favored acetone formation for **Cl. acetobutylicum**. Husernann et al 1988 found that acetoacetate addition increased the effect of undissociated butyric acid on the solventogenesis. How can we explain these results?

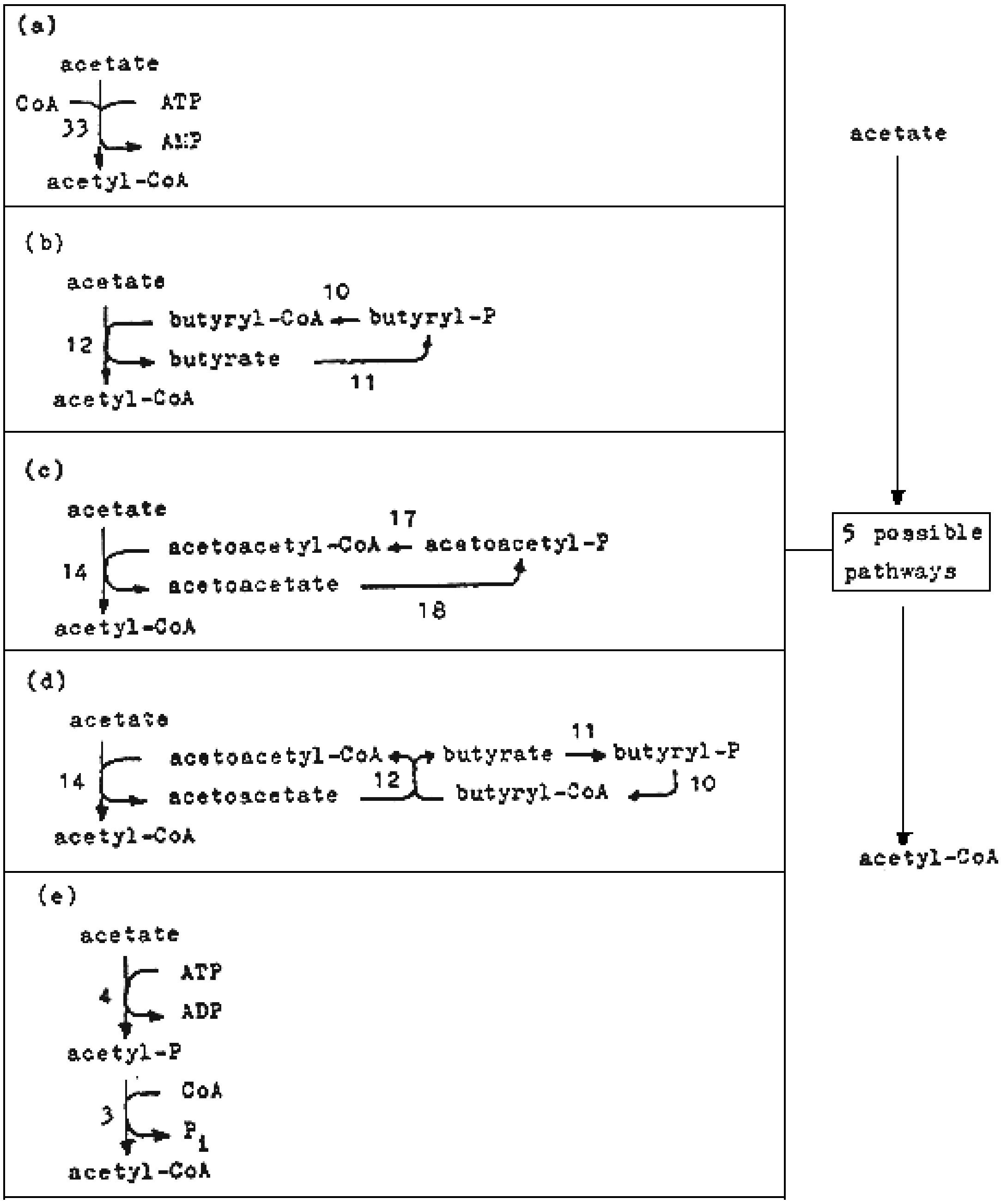


Figure 9 Five possible metabolic pathways for the formation of acetyl-CoA from acetate. The enzymes are mentioned in the preceeding figures, except (33) acetate : acetyl-CoA thiokinase.

Five different biochemical routes of acetate conversion to acetyl-CoA (Fig. 9) are proposed. Two of them (Fig. 9a and Fig. 9e) require ATP. Three of them require both ATP and catalytic amounts of the organic acids : butyrate loop (Fig. 9b), acetoacetate loop (Fig. 9c) and butyrate-acetoacetate loop (Fig. 9d). The existence of enzymes concerned is wellknown.

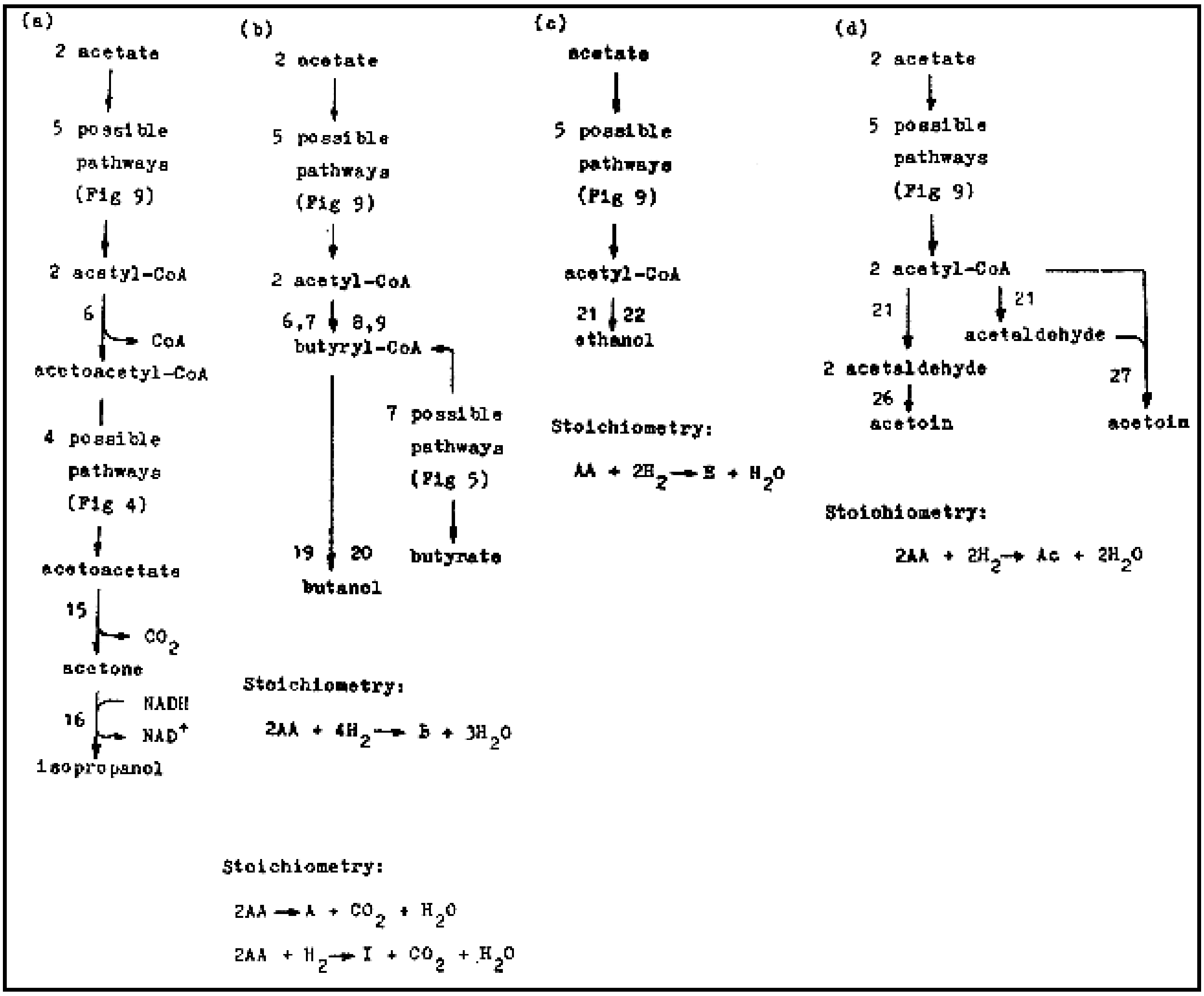


Figure 10 Metabolic units' and stoichiometries of solvents production from acetic acid at solventogenesis : (a) A/I from AA, (b) B from AA, (c) E from AA and (d) Ac from AA. The enzymes are mentioned in the preceeding figures.

Metabolic units of acetate conversion to neutral solvents are presented in Fig. 10. Acetone formation from acetate requires ATP while isopropanol formation requires both ATP and NADH (Fig. 10a). Butanol formation from acetate (Fig. 10b) needs ATP and NADH ; production of one mole of butanol requires four moles of NADH. Ethanol formation from acetate (Fig. 10c) and acetoin formation from acetate (Fig. 10d) require both ATP and NADH. Stoichiometries of these metabolic units are as follows :

For acetone formation from acetate,

$$2AA \longrightarrow A + CO_2 + H_2O \quad (15)$$

For isopropanol formation from acetate,

$$2AA + H_2 \longrightarrow I + CO\ 2 + H_2O \quad (16)$$

For butanol formation from acetate,

$$2AA + 4\ H_2 \longrightarrow B + 3\ H_2O \quad (17)$$

For ethanol formation from acetate,

$$AA + 2\ H_2 \longrightarrow E + H_2O \quad (18)$$

For acetoin formation from acetate,

$$2AA + 2\ H_2 \longrightarrow Ac + 2\ H_2O \quad (19)$$

Metabolic units of butyrate conversion to neutral solvents are presented in Fig. 11. Butanol formation from butyrate (Fig. 11a) requires both ATP and NADH. Acetone formation from butyrate and isopropanol formation from butyrate require ATP but produce NADH (Fig. 11b). Ethanol formation from butyrate (Fig.11e) and acetoin formation from butyrate (Fig. 11d) require both ATP and NADH. Stoichiometries of these metabolic units are as follows :

For butanot formation from butyrate,

$$BA + 2\ H_2 \longrightarrow B + H_2O \quad (20)$$

For acetone formation from butyrate,

$$BA + H_2O \longrightarrow A + CO_2 + 2\ H_2 \quad (21)$$

For isopropanol formation from butyrate,

$$BA + H_2O \longrightarrow I + CO_2 + H_2 \quad (22)$$

For ethanol formation from butyrate,

$$BA + 2\ H_2 \longrightarrow 2E \quad (23)$$

For acetoin formation from butyrate,

$$BA \longrightarrow Ac \quad (24)$$

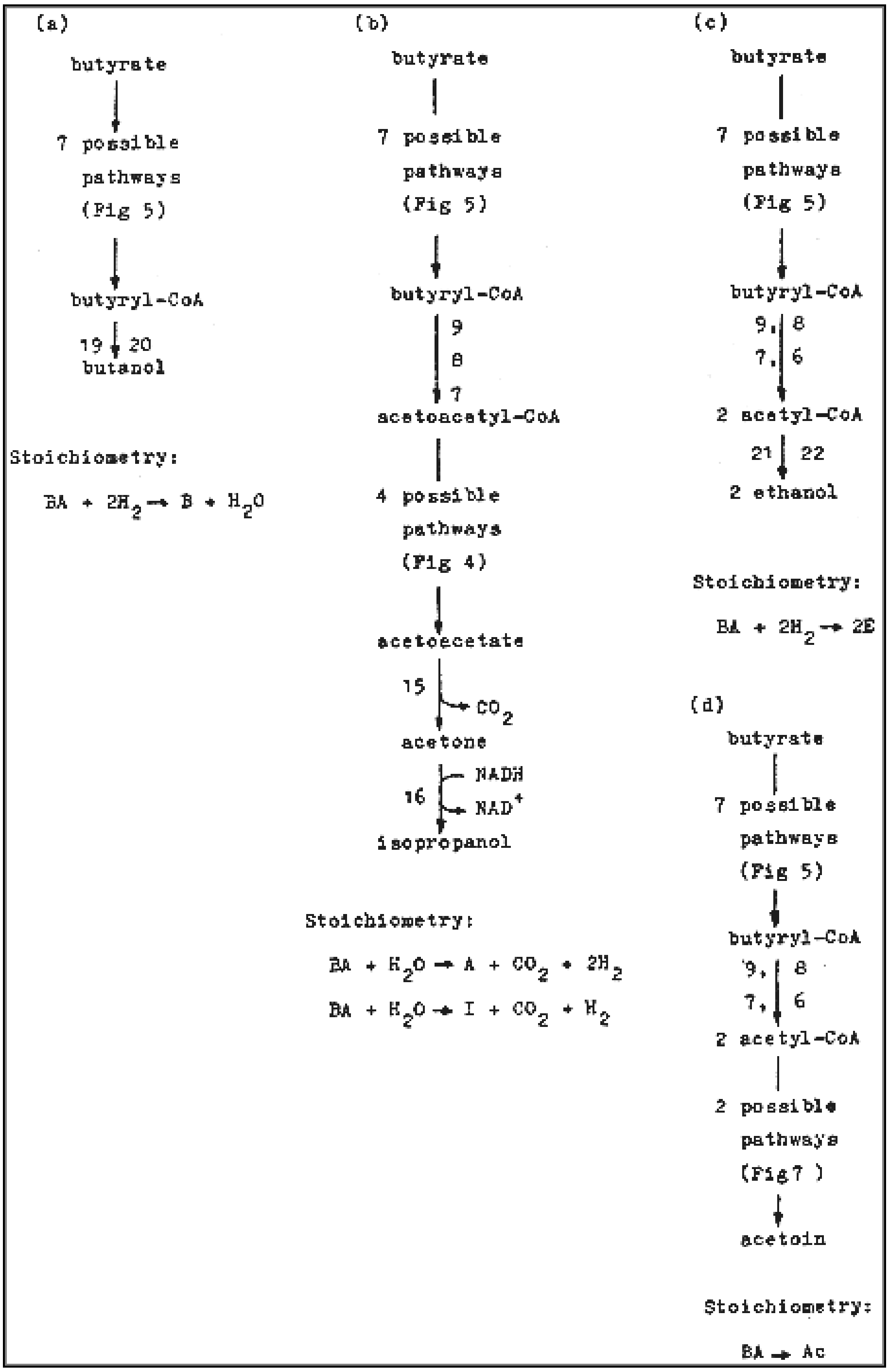


Figure 11 Metabolic units and stoichiometries of solvents production from butyric acid at solventogenesis : (a) B from BA, (b) A/I from BA, (c) E from BA and (d) Ac from BA. The enzymes are mentioned in the preceeding figures.

2.2.2.3 Metabolic Units of Solvents Formation from the Co-utilization of Glucose and Organic Acids

I. Metabolic Units of Solvents Formation from the Co-utilization of Glucose and Acetic Acid

There are 6 metabolic units of products formation from glucose previously mentioned : acetic acid formation (G $\longrightarrow$ 2AA), butyric acid formation (G $\longrightarrow$ BA), acetone/isopropanol formation (G$\longrightarrow$ A/I), butanol formation (G$\longrightarrow$ B), ethanol formation (G$\longrightarrow$ 2E) and acetoin formation (G $\longrightarrow$ Ac). Solvents formation from acetic acid has 4 metabolic units : acetone/isopropanol formation (2AA $\longrightarrow$ A/I), butanol formation (2AA $\longrightarrow$ B), ethanol formation (AA $\longrightarrow$ E) and acetoin formation (2AA $\longrightarrow$ Ac). Biochemical pathways arise from the co-utilization of glucose and acetic acid are analysed. Combinations of six metabolic units of products formation from glucose and four metabolic units of solvents formation from acetic acid give total possible metabolic units of 1013 cases (Table 4). Some of them are determined (Table 5). Stoichiometries corresponding to selected metabolic units are written (Table 6 and 7). Details of some metabolic units and their stoichiometries are presented (Fig. 12).

Table 4. Total numbers of metabolic units of co-substrates formed from the Combinations of individual metabolic units using glucose or acetic acid as a substrate.

Individual Metabolic units	Combinations	Total numbers of metabolic units of co-substractes formed from the combinations of	
		8 metabolic units	10 metabolic units
1. (G $\longrightarrow$ A/I)	2	16	24
2. (G $\longrightarrow$ B)	3	48	96
3. (G $\longrightarrow$ 2E)	4	100	1194
4. (G $\longrightarrow$ Ac)	5	56	246
5. (2AA $\longrightarrow$ A/I)	6	28	249
6. (2AA $\longrightarrow$ B)	7	8	120
7. (AA $\longrightarrow$ E)	8	1	45
8. (2AA $\longrightarrow$ Ac)	9	–	10
9. (G $\longrightarrow$ 2AA)	10	–	1
10. (G $\longrightarrow$ BA)			
Total cases	54	247	1,013

Table 5. Some metabolic units of co-substrates formed from the combinations of 10 individual metabolic units using glucose or acetic acid as a substrate.

2 Combination *24 cases*	*3 Combination* *somes of 96 cases*	*4 Combinations* *somes of 194 cases*
1. (G → 2AA) / (2AA → A / I)	(G → 2AA) / (G → BA) / (2AA → A / I)	(G → 2AA) / (G → BA) / (G → A / I) / (2AA → B)
2. (G → 2AA) / (2AA → B)	(G → 2AA) / (G → BA) / (2AA → B)	(G → 2AA) / (G → BA) / (G → B) / (2AA → A / I)
3. (G → 2AA) / (AA → E)	(G → 2AA) / (G → A / I) / (2AA → B)	(G → 2AA) / (G → BA) / (G → 2E) / (2AA → A / I)
4. (G → 2AA) / (2AA → Ac)	(G → 2AA) / (G → A / I) / (AA → E)	(G → 2AA) / (G → BA) / (G → Ac) / (2AA → B)
5. (G → BA) / (2AA → A/I)	(G → 2AA) / (G → B) / (2AA → A / I)	(G → 2AA) / (G → A / I) / (G → B) / (AA → E)
6. (G → BA) / (2AA → B)	(G → 2AA) / (G → B) / (AA → E)	(G → 2AA) / (G → B) / (G → 2E) / (2AA → A / I)
7. (G → BA) / (AA → E)	(G → 2AA) / (G → 2E) / (2AA → A / I)	(G → 2AA) / (G → 2E) / (G → Ac) / (2AA → B)
8. (G → BA) / (2AA → Ac)	(G → 2AA) / (G → 2E) / (2AA → B)	(G → BA) / (G → A / I) / (G → B) / (AA → E)
9. (G → A / I) / (2AA → A / I)	(G → 2AA) / (G → Ac) / (2AA → A / I)	(G → BA) / (G → B) / (G → 2E) / (2AA → A / I)
10. (G → A / I) / (2AA → E)	(G → BA) / (G → A / I) / (2AA → A / I)	(G → BA) / (G → 2E) / (G → Ac) / (2AA → Ac)
11. (G → A / I) / (AA → E)	(G → BA) / (G → A / I) / (2AA → B)	(G → A / I) / (G → B) / (G → 2E) / (2AA → A / I)
12. (G → A / I) / (2AA → Ac)	(G → BA) / (G → B) / (2AA → A / I)	(G → B) / (G → 2E) / (G → Ac) / (2AA → A / I)
13. (G → B) / (2AA → A / I)	(G → BA) / (G → B) / (2AA → Ac)	(G → 2AA) / (G → BA) / (2AA → A / I) / (2AA → B)
14. (G → B) / (2AA → E)	(G → BA) / (G → 2E) / (2AA → A / I)	(G → 2AA) / (G → A / I) / (2AA → B) / (AA → E)
15. (G → B) / (AA → E)	(G → BA) / (G → Ac) / (2AA → B)	(G → 2AA) / (G → B) / (2AA → A / I) / (AA → E)
16. (G → B) / (2AA → Ac)	(G → A / I) / (G → B) / (2AA → B)	(G → 2AA) / (G → 2E) / (2AA → A / I) / (2AA → B)
17. (G → 2E) / (2AA → A / I)	(G → A / I) / (G → B) / (AA → E)	(G → 2AA) / (G → Ac) / (2AA → A / I) / (2AA → Ac)
18. (G → 2E) / (2AA → B)	(G → A / I) / (G → 2E) / (2AA → B)	(G → BA) / (G → A / I) / (2AA → B) / (AA → E)
19. (G → 2E) / (AA → E)	(G → A / I) / (G → Ac) / (2AA → A / I)	(G → BA) / (G → B) / (2AA → A / I) / (2AA → B)
20. (G → 2E) / (2AA → Ac)	(G → B) / (G → 2E) / (2AA → A / I)	(G → BA) / (G → 2E) / (2AA → A / I) / (2AA → B)
21. (G → Ac) / (2AA → A / I)	(G → B) / (G → Ac) / (2AA → A / I)	(G → BA) / (G → Ac) / (2AA → A / I) / (2AA → Ac)
22. (G → Ac) / (2AA → B)	(G → 2AA) / (2AA → A / I) / (2AA → E)	(G → A / I) / (G → B) / (AA → E) / (2AA → Ac)
23. (G → Ac) / (AA → E)	(G → A / I) / (2AA → A / I) / (2AA → E)	(G → A / I) / (G → 2B) / (AA → E) / (2AA → B)
24. (G → Ac) / (2AA → Ac)	(G → 2AA) / (2AA → A / I) / (AA → E)	(G → B) / (G → 2E) / (2AA → A / I) / (2AA → Ac)
	(G → B) / (2AA → A / I) / (2AA → Ac)	(G → B) / (G → Ac) / (2AA → A / I) / (AA → E)
	(G → A / I) / (2AA → B) / (AA → E)	(G → 2E) / (G → Ac) / (2AA → A / I) / (2AA → B)
	(G → A / I) / (2AA → B) / (AA → Ac)	(G → 2AA) / (2AA → A / I) / (2AA → B) / (AA → E)
	(G → 2AA) / (AA → E) / (2AA → Ac)	(G → BA) / (2AA → A / I) / (2AA → B) / (2AA → Ac)
		(G → A / I) / (2AA → A / I) / (AA → E) / (2AA → Ac)
		(G → B) / (2AA → B) / (AA → E) / (2AA → Ac)
		(G → 2E) / (2AA → A / I) / (2AA → B) / (AA → E)
		(G → Ac) / (2AA → A / I) / (2AA → B) / (AA → E)

5 Combinations *somes of 246 cases*	*6 Combinations* *somes of 249 cases*
(G → 2AA) / (G → BA) / (G → A / I) / (G → B) / (2AA → B)	(G → 2AA) / (G → BA) / (G → A / I) / (G → B) / (G → 2E) / (2AA → A / I)
(G → 2AA) / (G → BA) / (G → A / I) / (G → 2E) / (AA → E)	(G → 2AA) / (G → BA) / (G → A / I) / (G → B) / (G → Ac) / (2AA → B)
(G → 2AA) / (G → BA) / (G → B) / (G → Ac) / (2AA → A / I)	(G → 2AA) / (G → BA) / (G → B) / (G → 2E) / (G → Ac) / (2AA → A / I)
(G → 2AA) / (G → A / I) / (G → B) / (G → 2E) / (2AA → B)	(G → 2AA) / (G → A / I) / (G → B) / (G → 2E) / (G → Ac) / (AA → E)
(G → 2AA) / (G → BA) / (G → 2E) / (G → Ac) / (2AA → A / I)	(G → BA) / (G → A / I) / (G → B) / (G → 2E) / (G → Ac) / (2AA → Ac)
(G → BA) / (G → A / I) / (G → B) / (G → 2E) / (2AA → Ac)	(G → 2AA) / (G → BA) / (G → A / I) / (G → B) / (2AA → A / I) / (2AA → B)
(G → BA) / (G → B) / (G → 2E) / (G → Ac) / (2AA → A / I)	(G → 2AA) / (G → BA) / (G → A / I) / (G → 2E) / (2AA → B) / (2AA → Ac)
(G → A / I) / (G → B) / (G → 2E) / (G → Ac) / (2AA → A / I)	(G → 2AA) / (G → BA) / (G → B) / (G → 2E) / (2AA → A / I) / (AA → E)
(G → 2AA) / (G → BA) / (G → A / I) / (2AA → A / I) / (2AA → B)	(G → 2AA) / (G → BA) / (G → 2E) / (G → Ac) / (2AA → A / I) / (2AA → B)
(G → 2AA) / (G → BA) / (G → B) / (2AA → A / I) / (AA → E)	(G → 2AA) / (G → A / I) / (G → B) / (G → 2E) / (2AA → B) / (AA → E)
(G → 2AA) / (G → A / I) / (G → B) / (2AA → B) / (AA → E)	(G → BA) / (G → A / I) / (G → 2E) / (G → Ac) / (2AA → A / I) / (2AA → B)
(G → 2AA) / (G → A / I) / (G → 2E) / (2AA → B) / (2AA → Ac)	(G → BA) / (G → A / I) / (G → B) / (G → 2E) / (2AA → B) / (AA → E)
(G → 2AA) / (G → B) / (G → 2E) / (2AA → A / I) / (2AA → B)	(G → A / I) / (G → B) / (G → 2E) / (G → Ac) / (2AA → A / I) / (AA → B)
(G → 2AA) / (G → B) / (G → Ac) / (2AA → A / I) / (AA → E)	(G → 2AA) / (G → BA) / (G → A / I) / (2AA → A / I) / (2AA → B) / (AA → B)
(G → BA) / (G → A / I) / (G → B) / (2AA → B) / (AA → E)	(G → 2AA) / (G → BA) / (G → B) / (2AA → A / I) / (AA → B) / (2AA → Ac)
(G → BA) / (G → B) / (G → 2E) / (2AA → A / I) / (2AA → B)	(G → 2AA) / (G → BA) / (G → 2E) / (2AA → A / I) / (2AA → B) / (2AA → Ac)
(G → BA) / (G → B) / (G → Ac) / (2AA → A / I) / (AA → E)	(G → 2AA) / (G → A / I) / (G → B) / (2AA → B) / (AA → E) / (2AA → Ac)
(G → A / I) / (G → B) / (G → 2E) / (2AA → A / I) / (2AA → B)	(G → 2AA) / (G → A / I) / (G → 2E) / (2AA → A / I) / (2AA → B) / (AA → E)
(G → A / I) / (G → B) / (G → 2E) / (2AA → A / I) / (AA → E)	(G → 2AA) / (G → B) / (G → 2E) / (2AA → A / I) / (AA → E) / (2AA → Ac)
(G → B) / (G → 2E) / (G → Ac) / (2AA → A / I) / (2AA → B)	(G → BA) / (G → A / I) / (G → B) / (2AA → A / I) / (2AA → B) / (AA → E)
(G → 2AA) / (G → BA) / (2AA → A / I) / (2AA → B) / (AA → E)	(G → BA) / (G → A / I) / (G → 2E) / (2AA → A / I) / (2AA → B) / (2AA → Ac)
(G → 2AA) / (G → A / I) / (2AA → A / I) / (2AA → B) / (AA → E)	(G → A / I) / (G → B) / (G → 2E) / (2AA → A / I) / (2AA → B) / (AA → E)
(G → 2AA) / (G → B) / (2AA → A / I) / (AA → E) / (2AA → Ac)	(G → A / I) / (G → 2E) / (G → Ac) / (2AA → B) / (AA → E) / (2AA → A / I)
(G → 2AA) / (G → 2E) / (2AA → A / I) / (2AA → B) / (AA → E)	(G → B) / (G → 2E) / (G → Ac) / (2AA → A / I) / (2AA → B) / (AA → E)
(G → BA) / (G → A / I) / (2AA → A / I) / (2AA → B) / (AA → E)	(G → 2AA) / (G → BA) / (2AA → A / I) / (2AA → B) / (AA → E) / (2AA → Ac)
(G → BA) / (G → B) / (2AA → B) / (AA → E) / (2AA → Ac)	(G → 2AA) / (G → A / I) / (2AA → A / I) / (2AA → B) / (AA → E) / (2AA → Ac)
(G → A / I) / (G → B) / (2AA → B) / (AA → E) / (2AA → Ac)	(G → 2AA) / (G → B) / (2AA → A / I) / (2AA → B) / (AA → E) / (2AA → Ac)
(G → A / I) / (G → 2E) / (2AA → A / I) / (2AA → B) / (2AA → Ac)	(G → BA) / (G → A / I) / (2AA → A / I) / (2AA → B) / (AA → E) / (2AA → Ac)
(G → B) / (G → 2E) / (2AA → A / I) / (2AA → E) / (AA → E)	(G → A / I) / (G → B) / (2AA → A / I) / (2AA → B) / (AA → E) / (2AA → Ac)
(G → 2AA) / (2AA → A / I) / (2AA → B) / (AA → E) / (2AA → Ac)	(G → A / I) / (G → 2E) / (2AA → A / I) / (2AA → B) / (AA → E) / (2AA → Ac)
(G → BA) / (2AA → A / I) / (2AA → B) / (AA → E) / (2AA → Ac)	
(G → A / I) / (2AA → A / I) / (2AA → B) / (AA → E) / (2AA → Ac)	

7 Combinations
somes of 120 cases
(G → 2AA) / (G → BA) / (G → A / I) / (G → B) / (G → 2E) / (G → Ac) / (2AA → A / I)
(G → 2AA) / (G → BA) / (G → A / I) / (G → B) / (G → 2E) / (G → Ac) / (2AA → B)
(G → 2AA) / (G → BA) / (G → A / I) / (G → B) / (G → 2E) / (G → Ac) / (AA → E)
(G → 2AA) / (G → BA) / (G → A / I) / (G → B) / (G → 2E) / (2AA → A / I) / (2AA → B)
(G → 2AA) / (G → BA) / (G → A / I) / (G → B) / (G → 2E) / (2AA → B) / (AA → E)
(G → 2AA) / (G → BA) / (G → A / I) / (G → 2E) / (G → Ac) / (2AA → B) / (2AA → Ac)
(G → 2AA) / (G → BA) / (G → B) / (G → 2E) / (G → Ac) / (2AA → A / I) / (2AA → B)
(G → 2AA) / (G → A / I) / (G → B) / (G → 2E) / (G → Ac) / (2AA → B) / (AA → E)
(G → BA) / (G → A / I) / (G → B) / (G → 2E) / (G → Ac) / (2AA → A / I) / (2AA → B)
(G → BA) / (G → A / I) / (G → B) / (G → 2E) / (G → Ac) / (2AA → B) / (AA → E)
(G → 2AA) / (G → BA) / (G → A / I) / (G → B) / (2AA → A / I) / (2AA → B) / (AA → E)
(G → 2AA) / (G → BA) / (G → A / I) / (G → B) / (2AA → B) / (AA → E) / (2AA → Ac)
(G → 2AA) / (G → BA) / (G → B) / (G → 2E) / (2AA → A / I) / (AA → E) / (2AA → Ac)
(G → 2AA) / (G → A / I) / (G → B) / (G → 2E) / (2AA → B) / (AA → E) / (2AA → Ac)
(G → BA) / (G → A / I) / (G → B) / (G → 2E) / (2AA → A / I) / (2AA → B) / (2AA → Ac)
(G → BA) / (G → A / I) / (G → B) / (G → Ac) / (2AA → A / I) / (2AA → B) / (AA → E)
(G → A / I) / (G → B) / (G → 2E) / (G → Ac) / (2AA → B) / (AA → E) / (2AA → Ac)
(G → 2AA) / (G → BA) / (G → A / I) / (2AA → A / I) / (2AA → B) / (AA → E) / (2AA → Ac)
(G → 2AA) / (G → BA) / (G → B) / (2AA → A / I) / (2AA → B) / (AA → E) / (2AA → Ac)
(G → 2AA) / (G → A / I) / (G → B) / (2AA → A / I) / (2AA → B) / (AA → E) / (2AA → Ac)
(G → BA) / (G → A / I) / (G → 2E) / (2AA → A / I) / (2AA → B) / (AA → E) / (2AA → Ac)
(G → BA) / (G → B) / (G → Ac) / (2AA → A / I) / (2AA → B) / (AA → E) / (2AA → Ac)
(G → A / I) / (G → B) / (G → 2E) / (2AA → A / I) / (2AA → B) / (AA → E) / (2AA → Ac)
(G → A / I) / (G → 2E) / (G → Ac) / (2AA → A / I) / (2AA → B) / (AA → E) / (2AA → Ac)
(G → B) / (G → 2E) / (G → Ac) / (2AA → A / I) / (2AA → B) / (AA → E) / (2AA → Ac)

8 Combinations

somesod 45 cases

(G → 2AA) / (G → BA) / (G → A / I) / (G → B) / (G → 2E) / (G → Ac) / (2AA → A / I) / (2AA → B)
(G → 2AA) / (G → BA) / (G → A / I) / (G → B) / (G → 2E) / (G → Ac) / (2AA → B) / (AA → E)
(G → 2AA) / (G → BA) / (G → A / I) / (G → B) / (G → 2E) / (2AA → A / I) / (2AA → B) / (AA → E)
(G → 2AA) / (G → BA) / (G → A / I) / (G → B) / (G → Ac) / (2AA → A / I) / (2AA → B) / (2AA → Ac)
(G → 2AA) / (G → BA) / (G → A / I) / (G → 2E) / (G → Ac) / (2AA → B) / (AA → E) / (2AA → Ac)
(G → BA) / (G → A / I) / (G → B) / (G → 2E) / (G → Ac) / (2AA → A / I) / (AA → E) / (2AA → Ac)
(G → 2AA) / (G → BA) / (G → A / I) / (G → B) / (2AA → A / I) / (2AA → B) / (AA → E) / (2AA → Ac)
(G → 2AA) / (G → BA) / (G → B) / (G → 2E) / (2AA → A / I) / (2AA → B) / (AA → E) / (2AA → Ac)
(G → BA) / (G → A / I) / (G → B) / (G → 2E) / (2AA → A / I) / (2AA → B) / (AA → E) / (2AA → Ac)
(G → BA) / (G → B) / (G → 2E) / (G → Ac) / (2AA → A / I) / (2AA → B) / (AA → E) / (2AA → Ac)
(G → A / I) / (G → B) / (G → 2E) / (G → Ac) / (2AA → A / I) / (2AA → B) / (AA → E) / (2AA → Ac)

9 Combinations

10 cases

(G → 2AA) / (G → BA) / (G → A / I) / (G → B) / (G → 2E) / (G → Ac) / (2AA → A / I) / (2AA → B) / (AA → E)
(G → 2AA) / (G → BA) / (G → A / I) / (G → B) / (G → 2E) / (G → Ac) / (2AA → A / I) / (2AA → B) / (2AA → Ac)
(G → 2AA) / (G → BA) / (G → A / I) / (G → B) / (G → 2E) / (G → Ac) / (2AA → A / I) / (AA → E) / (2AA → Ac)
(G → 2AA) / (G → BA) / (G → A / I) / (G → B) / (G → 2E) / (G → Ac) / (2AA → B) / (AA → E) / (2AA → Ac)
(G → 2AA) / (G → BA) / (G → A / I) / (G → B) / (G → 2E) / (2AA → A / I) / (2AA → B) / (AA → E) / (2AA → Ac)
(G → 2AA) / (G → BA) / (G → A / I) / (G → B) / (G → Ac) / (2AA → A / I) / (2AA → B) / (AA → E) / (2AA → Ac)
(G → 2AA) / (G → BA) / (G → A / I) / (G → 2E) / (G → Ac) / (2AA → A / I) / (2AA → B) / (AA → E) / (2AA → Ac)
(G → 2AA) / (G → BA) / (G → B) / (G → 2E) / (G → Ac) / (2AA → A / I) / (2AA → B) / (AA → E) / (2AA → Ac)
(G → 2AA) / (G → A / I) / (G → B) / (G → 2E) / (G → Ac) / (2AA → A / I) / (2AA → B) / (AA → E) / (2AA → Ac)
(G → BA) / (G → A / I) / (G → B) / (G → 2E) / (G → Ac) / (2AA → A / I) / (2AA → B) / (AA → E) / (2AA → Ac)

Table 6. Stoichiometries of representative metabolic units resulting from the combinations of (G → A/I) and (2AA → A/I), (2AA → B), (AA → E), (2AA → Ac).

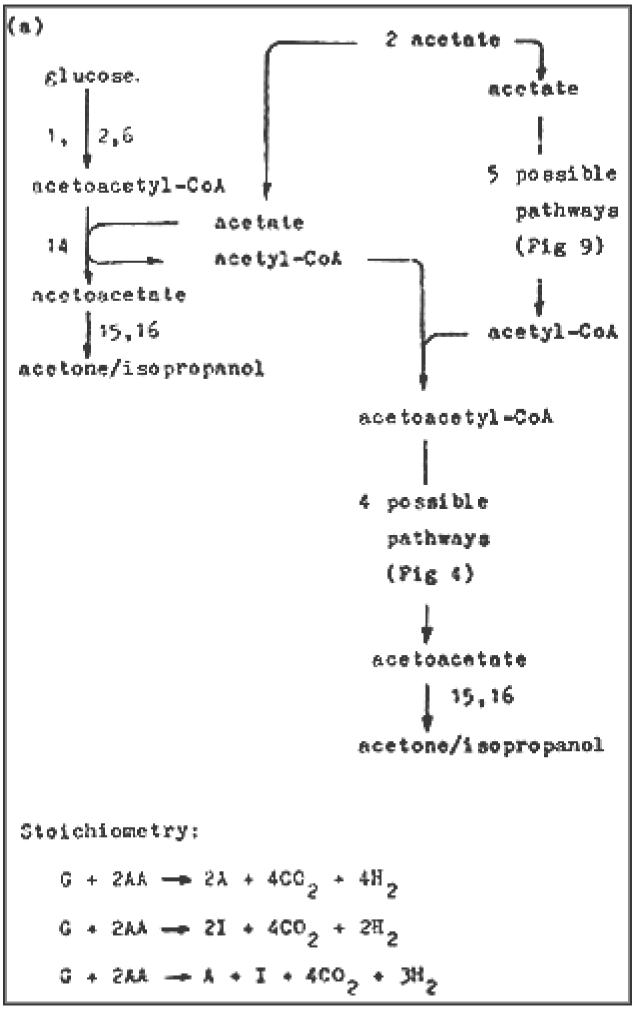
Metabolic units	Stoichiometries
1. (G → A/I) / (2AA → A/I)	$G + 2AA \rightarrow 2A + 4CO_2 + 4H_2$ $G + 2AA \rightarrow A + I + 4CO_2 + 3H_2$ $G + 2AA \rightarrow 2I + 4CO_2 + 2H_2$
2. (G → A/I) / (2AA → B)	$G + 2AA \rightarrow A + B + 3CO_2 + 2H_2O$ $G + 2AA \rightarrow H_2 \rightarrow I + B + 3CO_2 + 2H_2O$
3. (G → A/I) / (AA → E)	$G + AA \rightarrow A + E + 3CO_2 + 2H_2$ $G + AA \rightarrow I + E + 3CO_2 + H_2$
4. (G → A/I) / (2AA → Ac)	$G + 2AA \rightarrow A + Ac + 3CO_2 + 2H_2 + H_2O$ $G + 2AA \rightarrow I + Ac + 3CO_2 + H_2 + H_2O$
5. (G → A/I) / (2AA → A/I) (2AA → B)	$G + 4AA \rightarrow 2A + B + 4CO_2 + 3H_2O$ $G + 4AA + H_2 \rightarrow A + I + B + 4CO_2 + 3H_2O$ $G + 4AA + 2H_2 \rightarrow 2I + B + 4CO_2 + 3H_2O$
6. (G → A/I) / (2AA → A/I) (AA → E)	$G + 3AA \rightarrow 2A + E + 4CO_2 + 2H_2 + H_2O$ $G + 3AA \rightarrow A + I + E + 4CO_2 + H_2 + H_2O$ $G + 3AA \rightarrow 2I + E + 4CO_2 + H_2O$
7. (G → A/I) / (2AA → A/I) (2AA → Ac)	$G + 4AA \rightarrow 2A + Ac + 4CO_2 + 2H_2 + 2H_2O$ $G + 4AA \rightarrow A + I + Ac + 4CO_2 + H_2 + 2H_2O$ $G + 4AA \rightarrow 2I + Ac + 4CO_2 + 2H_2O$
8. (G → A/I) / (2AA → B) (AA → E)	$G + 3AA + 2H_2 \rightarrow A + B + E + 3CO_2 + 3H_2O$ $G + 3AA + 3H_2 \rightarrow I + B + E + 3CO_2 + 3H_2O$
9. (G → A/I) / (2AA → B) (2AA → Ac)	$G + 4AA + 2H_2 \rightarrow A + B + Ac + 3CO_2 + 4H_2O$ $G + 4AA + 3H_2 \rightarrow I + B + Ac + 3CO_2 + 4H_2O$
10. (G → A/I) / (AA → E) (2AA → Ac)	$G + 3AA \rightarrow A + E + Ac + 3CO_2 + 2H_2O$ $G + 3AA + H_2 \rightarrow I + E + Ac + 3CO_2 + 2H_2O$
11. (G → A/I) / (2AA → A / I) (2AA → B) / (AA → E)	$G + 5AA + 2H_2 \rightarrow 2A + B + E + 4CO_2 + 4H_2O$ $G + 5AA + 3H_2 \rightarrow A + I + B + E + 4CO_2 + 4H_2O$ $G + 5AA + 4H_2 \rightarrow 2I + B + E + 4CO_2 + 3H_2O$
12. (G → A/I) / (2AA → A / I) (2AA → B) / (2AA → Ac)	$G + 6AA + 2H_2 \rightarrow 2A + B + Ac + 4CO_2 + 5H_2O$ $G + 6AA + 3H_2 \rightarrow A + I + B + Ac + 4CO_2 + 5H_2O$ $G + 6AA + 4H_2 \rightarrow 2I + B + Ac + 4CO_2 + 5H_2O$
13. (G → A/I) / (2AA → A / I) (AA → E) / (2AA → Ac)	$G + 5AA \rightarrow 2A + E + Ac + 4CO_2 + 3H_2O$ $G + 5AA + H_2 \rightarrow A + I + Ac + 4CO_2 + 3H_2O$ $G + 5AA + 2H_2 \rightarrow 2I + E + Ac + 4CO_2 + 3H_2O$

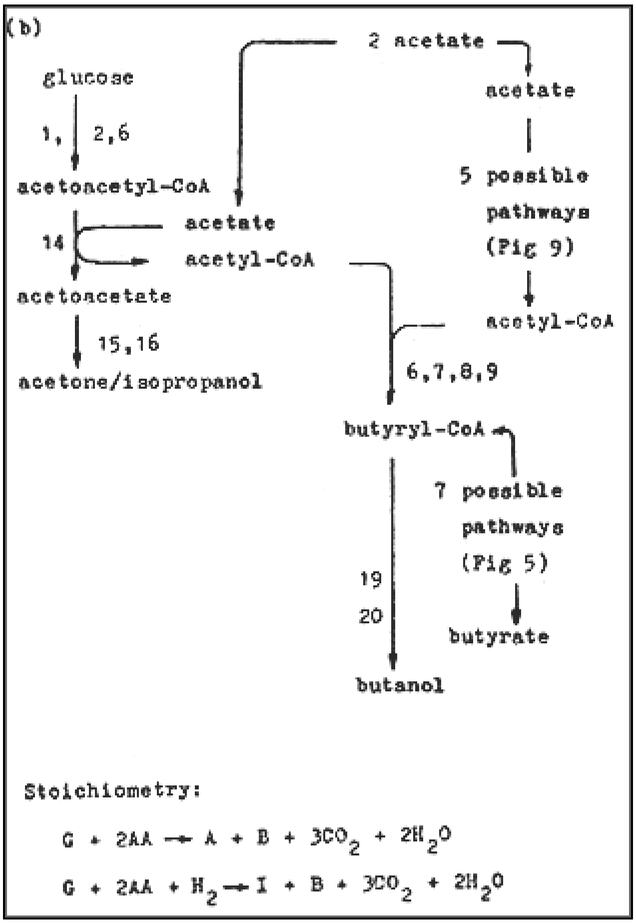
Metabolic units	Stoichiometries
14. $(G \rightarrow A/I) / (2AA \rightarrow B)$ $(AA \rightarrow E) / (2AA \rightarrow Ac)$	$G + 5AA + 4H_2 \rightarrow A + B + E + Ac + 3CO_2 + 5H_2O$ $G + 5AA + 4H_2 \rightarrow A + B + E + Ac + 3CO_2 + 5H_2O$ $G + 5AA + 5H_2 \rightarrow I + B + E + Ac + 3CO_2 + 5H_2O$
15. $(G \rightarrow A/I) / (2AA \rightarrow A/I)$ $(2AA \rightarrow B) / (AA \rightarrow E) /$ $(2AA \rightarrow Ac)$	$G + 7AA + 4H_2 \rightarrow 2A + B + E + Ac + 4CO_2 + 6H_2O$ $G + 7AA + 5H_2 \rightarrow A + I + B + E + Ac + 4CO_2 + 6H_2O$ $G + 7AA + 6H_2 \rightarrow 2I + B + E + Ac + 4CO_2 + 6H_2O$

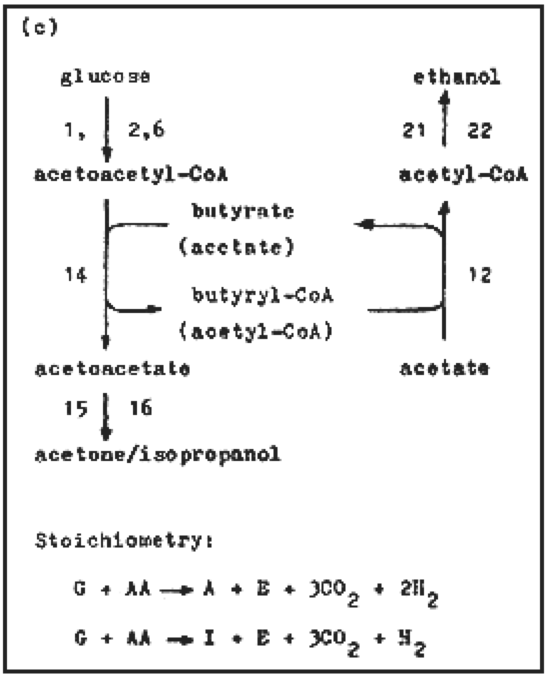
Table 7. Stoichiometries of representative metabolic units resulting from the combinations of $(G \rightarrow 2AA)$ and $(2AA \rightarrow A/I)$, $(2AA \rightarrow B)$, $(AA \rightarrow E)$, $(2AA \rightarrow Ac)$.

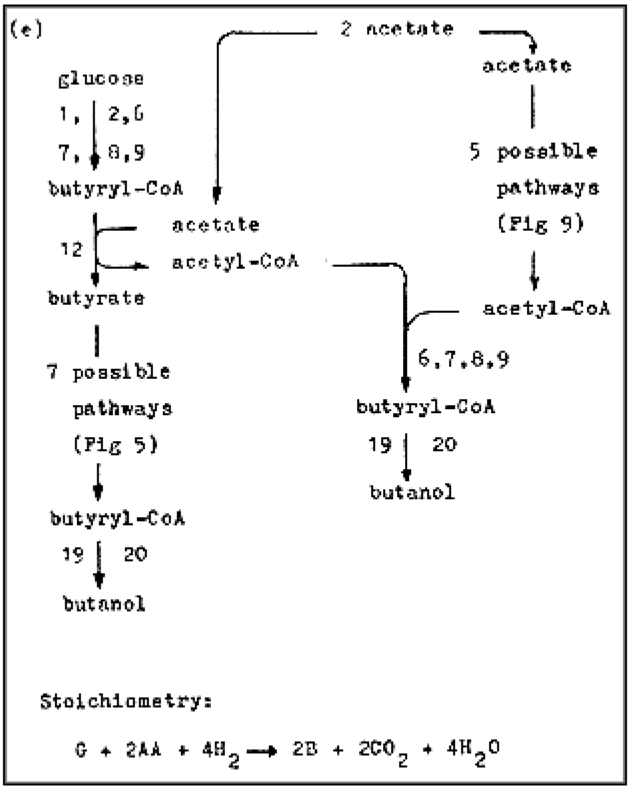
Metabolic units	Stoichiometries
1. $(G \rightarrow 2AA) / (2AA \rightarrow A/I)$	$G + H_2O \rightarrow A + 3CO_2 + 4H_2$ $G + H_2O \rightarrow I + 3CO_2 + 3H_2$ $G + 2AA \rightarrow A + I + 4CO_2 + 3H_2$
2. $(G \rightarrow 2AA) / (2AA \rightarrow B)$	$G \rightarrow B + 2CO_2 + H_2O$
3. $(G \rightarrow 2AA) / (AA \rightarrow E)$	$G + H_2O \rightarrow AA + E + 2CO_2 + 2H_2$
4. $(G \rightarrow 2AA) / (2AA \rightarrow Ac)$	$G \rightarrow Ac + 2CO_2 + 2H_2$
5. $(G \rightarrow 2AA) / (2AA \rightarrow A/I)$ $(2AA \rightarrow B)$	$G + 2AA \rightarrow A + B + 3CO_2 + 2H_2O$ $G + 2AA + H_2 \rightarrow I + B + 3CO_2 + 2H_2O$ $G + 4AA + H_2 \rightarrow A + I + B + 4CO_2 + 3H_2O$
6. $(G \rightarrow 2AA) / (2AA \rightarrow A/I)$ $(AA \rightarrow E)$	$G + AA \rightarrow A + E + 3CO_2 + 2H_2$ $G + AA \rightarrow I + E + 3CO_2 + H_2$ $G + 3AA \rightarrow A + I + E + 4CO_2 + H_2 + H_2O$
7. $(G \rightarrow 2AA) / (2AA \rightarrow A/I)$ $(2AA \rightarrow Ac)$	$G + 2AA \rightarrow A + Ac + 3CO_2 + 2H_2 + H_2O$ $G + 2AA \rightarrow I + Ac + 3CO_2 + H_2 + H_2O$ $G + 4AA \rightarrow A + I + Ac + 4CO_2 + H_2 + 2H_2O$
8. $(G \rightarrow 2AA) / (2AA \rightarrow B)$ $(AA \rightarrow E)$	$G + AA + 2H_2 \rightarrow B + E + 2CO_2 + 2H_2O$
9. $(G \rightarrow 2AA) / (2AA \rightarrow B)$ $(2AA \rightarrow Ac)$	$G + 2AA + 2H_2 \rightarrow B + Ac + 2CO_2 + 3H_2O$
10. $(G \rightarrow 2AA) / (AA \rightarrow E)$ $(2AA \rightarrow Ac)$	$G + AA \rightarrow E + Ac + 2CO_2 + H_2O$

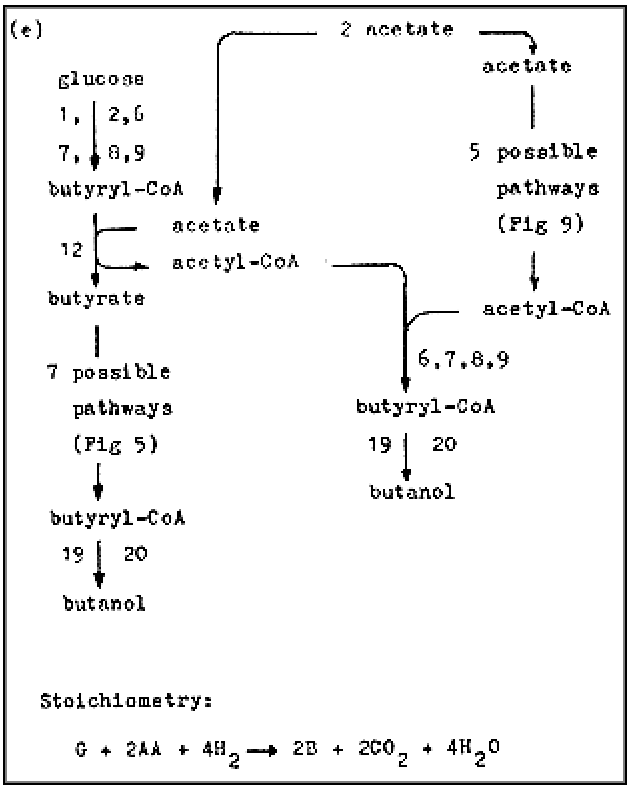
Metabolic units	Stoichiometries
11. (G $\rightarrow$ 2AA) / (2AA $\rightarrow$ A / I) (2AA $\rightarrow$ B) / (AA $\rightarrow$ E)	G + 3AA + $2H_2$ $\rightarrow$ A + B + E + $3CO_2$ + $3H_2O$ G + 3AA + $3H_2$ $\rightarrow$ I + B + E + $3CO_2$ + $3H_2O$ G + 5AA + $3H_2$ $\rightarrow$ A + I + B + E + $4CO_2$ + $4H_2O$
12. (G $\rightarrow$ 2AA) / (2AA $\rightarrow$ A / I) (2AA $\rightarrow$ B) / (2AA $\rightarrow$ Ac)	G + 4AA + $2H_2$ $\rightarrow$ A + B + Ac + $3CO_2$ + $4H_2O$ G + 4AA + $3H_2$ $\rightarrow$ I + B + Ac + $3CO_2$ + $4H_2O$ G + 6AA + $3H_2$ $\rightarrow$ A + I + B + Ac + $4CO_2$ + $5H_2O$
13. (G $\rightarrow$ 2AA) / (2AA $\rightarrow$ A / I) (AA $\rightarrow$ E) / (2AA $\rightarrow$ Ac)	G + 3AA $\rightarrow$ A + E + Ac + $3CO_2$ + $2H_2O$ G + 3AA + H_2 $\rightarrow$ I + E + Ac + $3CO_2$ + $2H_2O$ G + 5AA + H_2 $\rightarrow$ A + I + E + Ac + $4CO_2$ + $3H_2O$
14. (G $\rightarrow$ 2AA) / (2AA $\rightarrow$ B) (AA $\rightarrow$ E) / (2AA $\rightarrow$ Ac)	G + 3AA + $4H_2$ $\rightarrow$ B + E + Ac + $2CO_2$ + $4H_2O$
15. (G $\rightarrow$ 2AA) / (2AA $\rightarrow$ A / I) (2AA $\rightarrow$ B) / (AA $\rightarrow$ E) (2AA $\rightarrow$ Ac)	G + 5AA + $4H_2$ $\rightarrow$ A + B + E + Ac + $3CO_2$ + $5H_2O$ G + 5AA + $5H_2$ $\rightarrow$ I + B + E + Ac + $3CO_2$ + $5H_2O$ G + 7AA + $5H_2$ $\rightarrow$ A + I + B + E + Ac + $4CO_2$ + $6H_2O$


(a)
glucose
1, 2,6
acetoacetyl-CoA
14
acetoacetate
15,16
acetone/isopropanol
2 acetate
acetate
5 possible pathways (Fig 9)
acetyl-CoA
acetate
acetyl-CoA
acetoacetyl-CoA
4 possible pathways (Fig 4)
acetoacetate
15,16
acetone/isopropanol
Stoichiometry:
G + 2AA → 2A + 4CO2 + 4H2
G + 2AA → 2I + 4CO2 + 2H2
G + 2AA → A + I + 4CO2 + 3H2


(b)
glucose
1, 2,6
acetoacetyl-CoA
14
acetoacetate
15,16
acetone/isopropanol
2 acetate
acetate
5 possible pathways (Fig 9)
acetyl-CoA
acetate
acetyl-CoA
6,7,8,9
butyryl-CoA
7 possible pathways (Fig 5)
butyrate
19
20
butanol
Stoichiometry:
G + 2AA → A + B + 3CO2 + 2H2O
G + 2AA + H2 → I + B + 3CO2 + 2H2O


(c)
glucose
1, 2,6
acetoacetyl-CoA
14
butyrate (acetate)
butyryl-CoA (acetyl-CoA)
acetoacetate
15 16
acetone/isopropanol
ethanol
21 22
acetyl-CoA
12
acetate
Stoichiometry:
G + AA → A + B + 3CO2 + 2H2
G + AA → I + B + 3CO2 + H2


(e)
glucose
1, 2,6
7, 8,9
butyryl-CoA
12
butyrate
7 possible pathways (Fig 5)
butyryl-CoA
19 20
butanol
2 acetate
acetate
5 possible pathways (Fig 9)
acetyl-CoA
acetate
acetyl-CoA
6,7,8,9
butyryl-CoA
19 20
butanol
Stoichiometry:
G + 2AA + 4H2 → 2B + 2CO2 + 4H2O



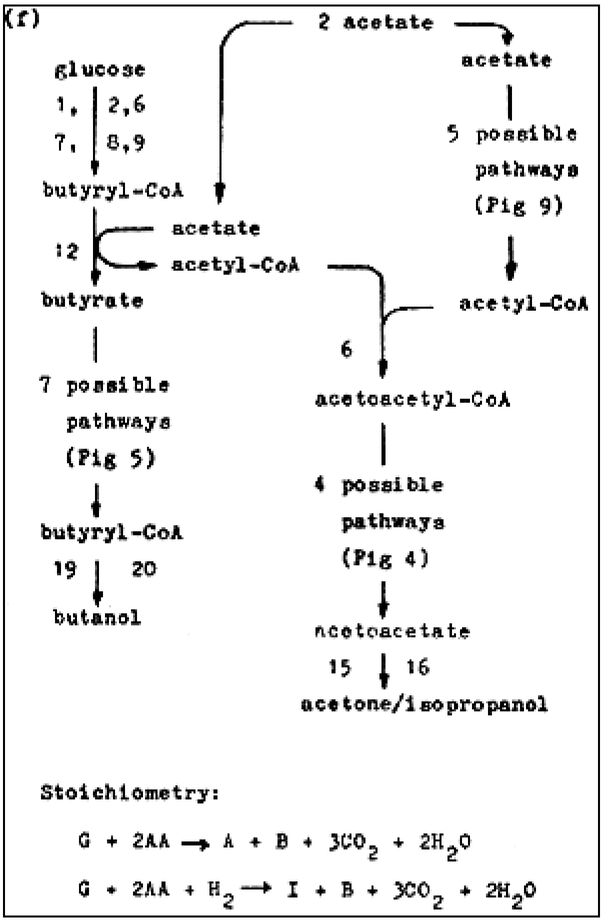


Figure 12 Metabolic units and stoichiometries of solvents formation from the co-utilization of glucose and acetic acid at solventogenesis :
(a) (G⟶ A/I) / (2AA ⟶ A/I), (b) (G⟶ A/I) / (2AA ⟶ B), (c) (G⟶ A/I) / (AA ⟶ E),
(d) (G ⟶ A/I) / (2AA ⟶ Ac), (e) (G ⟶ B) / (2AA ⟶ B), (f) (G ⟶ B) / (2AA ⟶ A/l)

II. Metabolic Units of Solvents Formation from the Co-utilization of Glucose and Butyric Acid

There are four metabolic units of solvents formation from butyric acid : butanol formation (BA⟶B), acetone / isopropanol formation (BA⟶A/1), ethanol formation (BA⟶2E) and acetoin formation (BA⟶Ac). Biochemical pathways of products formation using glucose and butyrate as co-substrates are analysed. Calculation by combination shows that there are 1,013 total cases for 10 pathways combinations (Table 8). Some of them are determined (Table 9). Stoichiometries corresponding to selected metabolic units are written (Table 10 and 11). Details of some metabolic units and their stoichiometries are presented (Fig. 13).

Table 8. Total numbers of metabolic units of co-substrates formed from the combinations of individual metabolic units.

Individual metabolic	Combinations	Total numbers of metabolic units of Co-substrates formed from the combinations of 8 metabolic units	Total numbers of metabolic units of Co-substrates formed from the combinations of 10 metabolic units
1. (G → A/I)	2	16	24
2. (G → B)	3	48	96
3. (G → 2E)	4	100	194
4. (G → Ac)	5	56	246
5. (BA → B)	6	28	249
6. (B → A/I)	7	8	120
7. (BA → 2E)	8	1	45
8. (BA → Ac)	9	-	10
9. (G → 2AA)	10	-	1
10. (G → BA)			
Total cases	54	247	1,013

Table 9. Some metabolic units of co-substrates formed from the combinations of 10 individual metabolic Units using glucose or butyric acid as a substrate

2 Combinations *24 cases*	*3 Combinations* *somes of 96 cases*
(G $\rightarrow$ 2AA) / (BA $\rightarrow$ B)	(G $\rightarrow$ 2AA) / (G $\rightarrow$ BA) / (BA $\rightarrow$ B)
(G $\rightarrow$ 2AA) / (BA $\rightarrow$ A / I)	(G $\rightarrow$ 2AA) / (G $\rightarrow$ A / I) / (BA $\rightarrow$ B)
(G $\rightarrow$ 2AA) / (BA $\rightarrow$ 2E)	(G $\rightarrow$ 2AA) / (G $\rightarrow$ B) / (BA $\rightarrow$ A / I)
(G $\rightarrow$ 2AA) / (BA $\rightarrow$ Ac)	(G $\rightarrow$ 2AA) / (G $\rightarrow$ 2E) / (BA $\rightarrow$ A / I)
(G $\rightarrow$ BA) / (BA $\rightarrow$ B)	(G $\rightarrow$ 2AA) / (G $\rightarrow$ Ac) / (BA $\rightarrow$ 2E)
(G $\rightarrow$ BA) / (BA $\rightarrow$ A / I)	(G $\rightarrow$ BA) / (G $\rightarrow$ A / I) / (BA $\rightarrow$ Ac)
(G $\rightarrow$ BA) / (BA $\rightarrow$ 2E)	(G $\rightarrow$ BA) / (G $\rightarrow$ B) / (BA $\rightarrow$ A / I)
(G $\rightarrow$ BA) / (BA $\rightarrow$ Ac)	(G $\rightarrow$ BA) / (G $\rightarrow$ 2E) / (BA $\rightarrow$ A / I)
(G $\rightarrow$ A / I) / (BA $\rightarrow$ B)	(G $\rightarrow$ BA) / (G $\rightarrow$ Ac) / (BA $\rightarrow$ B)
(G $\rightarrow$ A / I) / (BA $\rightarrow$ A / I)	(G $\rightarrow$ A / I) / (G $\rightarrow$ B) / (BA $\rightarrow$ B)
(G $\rightarrow$ A / I) / (BA $\rightarrow$ 2E)	(G $\rightarrow$ A / I) / (G $\rightarrow$ B) / (BA $\rightarrow$ 2E)
(G $\rightarrow$ A / I) / (BA $\rightarrow$ Ac)	(G $\rightarrow$ A / I) / (G $\rightarrow$ 2E) / (BA $\rightarrow$ B)
(G $\rightarrow$ B) / (BA $\rightarrow$ B)	(G $\rightarrow$ A / I) / (G $\rightarrow$ Ac) / (BA $\rightarrow$ 2E)
(G $\rightarrow$ B) / (BA $\rightarrow$ A / I)	(G $\rightarrow$ 2AA) / (BA $\rightarrow$ B) / (BA $\rightarrow$ A / I)
(G $\rightarrow$ B) / (BA $\rightarrow$ 2E)	(G $\rightarrow$ A / I) / (BA $\rightarrow$ B) / (BA $\rightarrow$ A / I)
(G $\rightarrow$ B) / (BA $\rightarrow$ Ac)	(G $\rightarrow$ 2AA) / (BA $\rightarrow$ B) / (BA $\rightarrow$ 2E)
(G $\rightarrow$ 2E) / (BA $\rightarrow$ B)	(G $\rightarrow$ A / I) / (BA $\rightarrow$ B) / (BA $\rightarrow$ 2E)
(G $\rightarrow$ 2E) / (BA $\rightarrow$ A / I)	(G $\rightarrow$ 2AA) / (BA $\rightarrow$ B) / (BA $\rightarrow$ Ac)
(G $\rightarrow$ 2E) / (BA $\rightarrow$ 2E)	(G $\rightarrow$ A / I) / (BA $\rightarrow$ B) / (BA $\rightarrow$ Ac)
(G $\rightarrow$ 2E) / (BA $\rightarrow$ Ac)	(G $\rightarrow$ 2AA) / (BA $\rightarrow$ A / I) / (BA $\rightarrow$ 2E)
(G $\rightarrow$ Ac) / (BA $\rightarrow$ B)	(G $\rightarrow$ A / I) / (BA $\rightarrow$ A / I) / (BA $\rightarrow$ 2E)
(G $\rightarrow$ Ac) / (BA $\rightarrow$ A / I)	(G $\rightarrow$ 2AA) / (BA $\rightarrow$ A / I) / (BA $\rightarrow$ Ac)
(G $\rightarrow$ Ac) / (BA $\rightarrow$ 2E)	(G $\rightarrow$ A / I) / (BA $\rightarrow$ A / I) / (BA $\rightarrow$ Ac)
(G $\rightarrow$ Ac) / (BA $\rightarrow$ Ac)	(G $\rightarrow$ 2AA) / (BA $\rightarrow$ 2E) / (BA $\rightarrow$ Ac)

4 Combinations *somes of 194 cases*	*5 Combinations* *somes of 246 cases*
(G → 2AA) / (G → BA) / (G → A / I) / (BA → B)	(G → 2AA) / (G → BA) / (G → A / I) / (G → B) / (BA → B)
(G → 2AA) / (G → BA) / (G → A / I) / (BA → 2E)	(G → 2AA) / (G → BA) / (G → A / I) / (G → 2E) / (BA → B)
(G → 2AA) / (G → BA) / (G → B) / (BA → 2E)	(G → 2AA) / (G → BA) / (G → B) / (G → 2E) / (BA → A / I)
(G → 2AA) / (G → A / I) / (G → B) / (BA → Ac)	(G → 2AA) / (G → BA) / (G → 2E) / (G → Ac) / (BA → A / I)
(G → 2AA) / (G → B) / (G → 2E) / (BA → A / I)	(G → 2AA) / (G → A / I) / (G → B) / (G → 2E) / (BA → 2E)
(G → 2AA) / (G → A / I) / (G → B) / (BA → B)	(G → 2AA) / (G → A / I) / (G → B) / (G → Ac) / (BA → 2E)
(G → 2AA) / (G → B) / (G → 2E) / (BA → A / I)	(G → 2AA) / (G → B) / (G → 2E) / (G → Ac) / (BA → A / I)
(G → BA) / (G → A / I) / (G → B) / (BA → 2E)	(G → BA) / (G → A / I) / (G → B) / (G → 2E) / (BA → Ac)
(G → BA) / (G → B) / (G → 2E) / (BA → A / I)	(G → A / I) / (G → B) / (G → 2E) / (G → Ac) / (BA → B)
(G → A / I) / (G → B) / (G → 2E) / (BA → Ac)	(G → 2AA) / (G → BA) / (G → A / I) / (BA → B) / (BA → A / I)
(G → A / I) / (G → 2E) / (G → Ac) / (BA → B)	(G → 2AA) / (G → BA) / (G → B) / (BA → A / I) / (BA → 2E)
(G → 2AA) / (G → BA) / (BA → B) / (BA → A / I)	(G → 2AA) / (G → A / I) / (G → B) / (BA → B) / (BA → 2E)
(G → 2AA) / (G → A / I) / (G → B) / (BA → 2E)	(G → 2AA) / (G → B) / (G → 2E) / (BA → A / I) / (BA → Ac)
(G → 2AA) / (G → B) / (BA → A / I) / (BA → 2E)	(G → BA) / (G → A / I) / (G → B) / (BA → B) / (BA → Ac)
(G → 2AA) / (G → 2E) / (BA → B) / (BA → A / I)	(G → A / I) / (G → B) / (G → 2E) / (BA → 2E) / (BA → Ac)
(G → BA) / (G → A / I) / (BA → 2E) / (BA → Ac)	(G → 2AA) / (G → BA) / (BA → B) / (BA → A / I) / (BA → 2E)
(G → BA) / (G → B) / (BA → A / I) / (BA → 2E)	(G → 2AA) / (G → BA) / (BA → B) / (BA → A / I) / (BA → 2E)
(G → A / I) / (G → B) / (BA → 2E) / (BA → Ac)	(G → 2AA) / (G → B) / (BA → A / I) / (BA → 2E) / (BA → Ac)
(G → A / I) / (G → 2E) / (BA → B) / (BA → A / I)	(G → BA) / (G → A / I) / (BA → B) / (BA → A / I) / (BA → 2E)
(G → 2AA) / (BA → B) / (BA → A / I) / (BA → 2E)	(G → A / I) / (G → B) / (BA → B) / (BA → A / I) / (BA → Ac)
(G → 2AA) / (BA → A / I) / (BA → 2E) / (BA → Ac)	(G → A / I) / (G → Ac) / (BA → B) / (BA → 2E) / (BA → Ac)
(G → BA) / (BA → B) / (BA → 2E) / (BA → Ac)	(G → 2AA) / (BA → B) / (BA → A / I) / (BA → 2E) / (BA → Ac)
(G → A / I) / (BA → B) / (BA → A / I) / (BA → Ac)	(G → BA) / (BA → B) / (BA → A / I) / (BA → 2E) / (BA → Ac)
(G → A / I) / (BA → A / I) / (BA → 2E) / (BA → Ac)	(G → A / I) / (BA → B) / (BA → A / I) / (BA → 2E) / (BA → Ac)
(G → B) / (BA → B) / (BA → A / I) / (BA → 2E)	(G → B) / (BA → B) / (BA → A / I) / (BA → 2E) / (BA → Ac)

6 Combinations *somes of 249 cases*
(G → 2AA) / (G → BA) / (G → A / I) / (G → B) / (G → 2E) / (BA → B)
(G → 2AA) / (G → BA) / (G → A / I) / (G → B) / (G → Ac) / (BA → A / I)
(G → 2AA) / (G → A / I) / (G → B) / (G → 2E) / (G → Ac) / (BA → 2E)
(G → BA) / (G → A / I) / (G → B) / (G → 2E) / (G → Ac) / (BA → Ac)
(G → 2AA) / (G → BA) / (G → A / I) / (G → B) / (BA → B) / (BA → A / I)
(G → 2AA) / (G → BA) / (G → A / I) / (G → 2E) / (BA → A / I) / (BA → 2E)
(G → 2AA) / (G → A / I) / (G → B) / (G → 2E) / (BA → A / I) / (BA → Ac)
(G → 2AA) / (G → A / I) / (G → 2E) / (G → Ac) / (BA → B) / (BA → A / I)
(G → BA) / (G → A / I) / (G → B) / (G → 2E) / (BA → B) / (BA → 2E)
(G → BA) / (G → A / I) / (G → 2E) / (G → Ac) / (BA → B) / (BA → Ac)
(G → BA) / (G → B) / (G → 2E) / (G → Ac) / (BA → A / I) / (BA → 2E)
(G → A / I) / (G → B) / (G → 2E) / (G → Ac) / (BA → B) / (BA → 2E)
(G → 2AA) / (G → BA) / (G → A / I) / (BA → B) / (BA → A / I) / (BA → 2E)
(G → 2AA) / (G → BA) / (G → B) / (BA → A / I) / (BA → 2E) / (BA → Ac)
(G → 2AA) / (G → BA) / (G → 2E) / (BA → B) / (BA → A / I) / (BA → 2E)
(G → 2AA) / (G → A / I) / (G → B) / (BA → A / I) / (BA → 2E) / (BA → Ac)
(G → 2AA) / (G → A / I) / (G → 2E) / (BA → B) / (BA → A / I) / (BA → Ac)
(G → 2AA) / (G → B) / (G → 2E) / (BA → A / I) / (BA → 2E) / (BA → Ac)
(G → 2AA) / (G → 2E) / (G → Ac) / (BA → A / I) / (BA → B) / (BA → 2E)
(G → BA) / (G → A / I) / (G → B) / (BA → B) / (BA → A / I) / (BA → Ac)
(G → BA) / (G → A / I) / (G → 2E) / (BA → B) / (BA → 2E) / (BA → Ac)
(G → BA) / (G → B) / (G → 2E) / (BA → A / I) / (BA → B) / (BA → 2E)
(G → A / I) / (G → B) / (G → 2E) / (BA → B) / (BA → 2E) / (BA → Ac)
(G → A / I) / (G → 2E) / (G → Ac) / (BA → B) / (BA → A / I) / (BA → 2E)
(G → 2AA) / (G → BA) / (BA → B) / (BA → A / I) / (BA → 2E) / (BA → Ac)
(G → 2AA) / (G → A / I) / (BA → B) / (BA → A / I) / (BA → 2E) / (BA → Ac)
(G → BA) / (G → A / I) / (BA → B) / (BA → A / I) / (BA → 2E) / (BA → Ac)
(G → BA) / (G → B) / (BA → B) / (BA → A / I) / (BA → 2E) / (BA → Ac)
(G → A / I) / (G → B) / (BA → B) / (BA → A / I) / (BA → 2E) / (BA → Ac)
(G → A / I) / (G → 2E) / (BA → B) / (BA → A / I) / (BA → 2E) / (BA → Ac)

7 Combinations *somes of 120 cases*
(G → 2AA) / (G → BA) / (G → A / I) / (G → B) / (G → 2E) / (G → Ac) / (BA → B)
(G → 2AA) / (G → BA) / (G → A / I) / (G → B) / (G → 2E) / (G → Ac) / (BA → A / I)
(G → 2AA) / (G → BA) / (G → A / I) / (G → B) / (G → 2E) / (BA → B) / (BA → A / I)
(G → 2AA) / (G → BA) / (G → A / I) / (G → B) / (G → Ac) / (BA → 2E) / (BA → Ac)
(G → 2AA) / (G → A / I) / (G → B) / (G → 2E) / (G → Ac) / (BA → B) / (BA → 2E)
(G → BA) / (G → A / I) / (G → B) / (G → 2E) / (G → Ac) / (BA → A / I) / (BA → Ac)
(G → 2AA) / (G → BA) / (G → A / I) / (G → B) / (BA → B) / (BA → A / I) / (BA → 2E)
(G → 2AA) / (G → BA) / (G → A / I) / (G → 2E) / (BA → A / I) / (BA → 2E) / (BA → Ac)
(G → 2AA) / (G → BA) / (G → B) / (G → 2E) / (BA → B) / (BA → A / I) / (BA → 2E)
(G → 2AA) / (G → BA) / (G → 2E) / (G → Ac) / (BA → A / I) / (BA → B) / (BA → 2E)
(G → 2AA) / (G → A / I) / (G → B) / (G → 2E) / (BA → B) / (BA → 2E) / (BA → Ac)
(G → 2AA) / (G → A / I) / (G → 2E) / (G → Ac) / (BA → B) / (BA → A / I) / (BA → 2E)
(G → 2AA) / (G → B) / (G → 2E) / (G → Ac) / (BA → A / I) / (BA → 2E) / (BA → Ac)
(G → BA) / (G → A / I) / (G → B) / (G → 2E) / (BA → B) / (BA → A / I) / (BA → 2E)
(G → BA) / (G → A / I) / (G → 2E) / (G → Ac) / (BA → B) / (BA → A / I) / (BA → 2E)
(G → A / I) / (G → B) / (G → 2E) / (G → Ac) / (BA → B) / (BA → 2E) / (BA → Ac)
(G → A / I) / (G → B) / (G → 2E) / (G → Ac) / (BA → B) / (BA → A / I) / (BA → 2E)
(G → 2AA) / (G → BA) / (G → A / I) / (BA → B) / (BA → A / I) / (BA → 2E) / (BA → Ac)
(G → 2AA) / (G → BA) / (G → B) / (BA → B) / (BA → A / I) / (BA → 2E) / (BA → Ac)
(G → 2AA) / (G → A / I) / (G → B) / (BA → B) / (BA → A / I) / (BA → 2E) / (BA → Ac)
(G → 2AA) / (G → A / I) / (G → 2E) / (BA → B) / (BA → A / I) / (BA → 2E) / (BA → Ac)
(G → 2AA) / (G → B) / (G → 2E) / (BA → B) / (BA → A / I) / (BA → 2E) / (BA → Ac)
(G → 2AA) / (G → 2E) / (G → Ac) / (BA → B) / (BA → A / I) / (BA → 2E) / (BA → Ac)
(G → BA) / (G → A / I) / (G → B) / (BA → B) / (BA → A / I) / (BA → 2E) / (BA → Ac)
(G → BA) / (G → A / I) / (G → 2E) / (BA → B) / (BA → A / I) / (BA → 2E) / (BA → Ac)
(G → BA) / (G → B) / (G → 2E) / (BA → B) / (BA → A / I) / (BA → 2E) / (BA → Ac)
(G → A / I) / (G → B) / (G → 2E) / (BA → B) / (BA → A / I) / (BA → 2E) / (BA → Ac)
(G → A / I) / (G → 2E) / (G → Ac) / (BA → B) / (BA → A / I) / (BA → 2E) / (BA → Ac)

8 Combinations *somes of 45 cases*
(G → 2AA) / (G → BA) / (G → A / I) / (G → B) / (G → 2E) / (G → Ac) / (BA → B) / (BA → A / I)
(G → 2AA) / (G → BA) / (G → A / I) / (G → B) / (G → 2E) / (G → Ac) / (BA → B) / (BA → 2E)
(G → 2AA) / (G → BA) / (G → A / I) / (G → B) / (G → 2E) / (G → Ac) / (BA → A / I) / (BA → 2E)
(G → 2AA) / (G → BA) / (G → A / I) / (G → B) / (G → 2E) / (BA → B) / (BA → A / I) / (BA → 2E)
(G → 2AA) / (G → BA) / (G → A / I) / (G → 2E) / (G → Ac) / (BA → B) / (BA → 2E) / (BA → Ac)
(G → 2AA) / (G → BA) / (G → B) / (G → 2E) / (G → 2E) / (G → Ac) / (BA → B) / (BA → 2E)
(G → 2AA) / (G → A / I) / (G → B) / (G → 2E) / (G → Ac) / (BA → B) / (BA → A / I) / (BA → Ac)
(G → BA) / (G → A / I) / (G → B) / (G → 2E) / (G → Ac) / (BA → B) / (BA → A / I) / (BA → 2E)
(G → 2AA) / (G → BA) / (G → B) / (G → 2E) / (BA → B) / (BA → A / I) / (BA → 2E) / (BA → Ac)
(G → 2AA) / (G → BA) / (G → A / I) / (G → B) / (BA → B) / (BA → A / I) / (BA → 2E) / (BA → Ac)
(G → 2AA) / (G → A / I) / (G → 2E) / (G → Ac) / (BA → B) / (BA → A / I) / (BA → 2E) / (BA → Ac)
(G → BA) / (G → A / I) / (G → B) / (G → 2E) / (BA → B) / (BA → A / I) / (BA → 2E) / (BA → Ac)
(G → A / I) / (G → B) / (G → 2E) / (G → Ac) / (BA → B) / (BA → A / I) / (BA → 2E) / (BA → Ac)

9 Combinations *10 cases*
(G → 2AA) / (G → BA) / (G → A / I) / (G → B) / (G → 2E) / (G → Ac) / (BA → B) / (BA → A / I) / (BA → 2E)
(G → 2AA) / (G → BA) / (G → A / I) / (G → B) / (G → 2E) / (G → Ac) / (BA → B) / (BA → A / I) / (BA → Ac)
(G → 2AA) / (G → BA) / (G → A / I) / (G → B) / (G → 2E) / (G → Ac) / (BA → B) / (BA → 2E) / (BA → Ac)
(G → 2AA) / (G → BA) / (G → A / I) / (G → B) / (G → 2E) / (G → Ac) / (BA → A / I) / (BA → 2E) / (BA → Ac)
(G → 2AA) / (G → BA) / (G → A / I) / (G → B) / (G → 2E) / (BA → B) / (BA → A / I) / (BA → 2E) / (BA → Ac)
(G → 2AA) / (G → BA) / (G → A / I) / (G → B) / (G → Ac) / (BA → B) / (BA → A / I) / (BA → 2E) / (BA → Ac)
(G → 2AA) / (G → BA) / (G → A / I) / (G → 2E) / (G → Ac) / (BA → B) / (BA → A / I) / (BA → 2E) / (BA → Ac)
(G → 2AA) / (G → BA) / (G → B) / (G → 2E) / (G → Ac) / (BA → B) / (BA → A / I) / (BA → 2E) / (BA → Ac)
(G → 2AA) / (G → A / I) / (G → B) / (G → 2E) / (G → Ac) / (BA → B) / (BA → A / I) / (BA → 2E) / (BA → Ac)
(G → BA) / (G → A / I) / (G → B) / (G → 2E) / (G → Ac) / (BA → B) / (BA → A / I) / (BA → 2E) / (BA → Ac)

Table 10. Stoichiometries of representative metabolic units resulting from the combinations of ($G \rightarrow A / I$) coupled with ($BA \rightarrow B$), ($BA \rightarrow A/I$), ($BA \rightarrow 2E$) and ($BA \rightarrow Ac$).

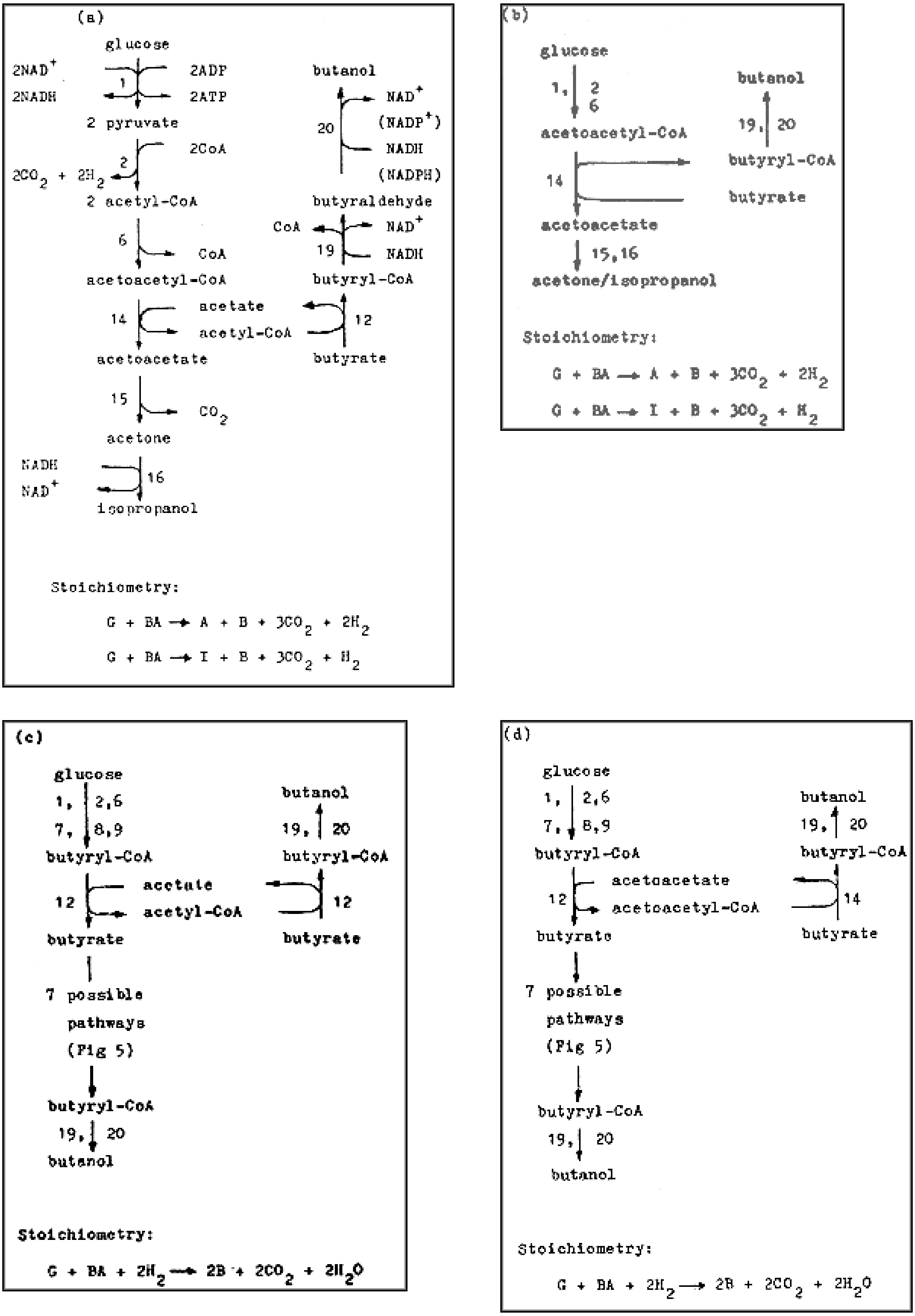
Metabolic units	Stoichiometries
1. $(G \rightarrow A / I) / (BA \rightarrow B)$	$G + BA \rightarrow A + B + 3CO_2 + 2H_2$ $G + BA \rightarrow I + B + 3CO_2 + H_2$
2. $(G \rightarrow A / I) / (BA \rightarrow A / I)$	$G + BA + 2H_2O \rightarrow 2A + 4CO_2 + 6H_2$ $G + BA + 2H_2O \rightarrow A + I + 4CO_2 + 5H_2$ $G + BA + 2H_2O \rightarrow 2I + 4CO_2 + 4H_2$
3. $(G \rightarrow A / I) / (BA \rightarrow 2E)$	$G + BA + H_2O \rightarrow A + 2E + 3CO_2 + 2H_2$ $G + BA + H_2O \rightarrow 1 + 2E + 3CO_2 + H_2$
4. $(G \rightarrow A / I) / (BA \rightarrow Ac)$	$G + BA + H_2O \rightarrow A + Ac + 3CO_2 + 4H_2$ $G + BA + H_2O \rightarrow 1 + Ac + 3CO_2 + 3H_2$
5. $(G \rightarrow A / I) / (BA \rightarrow B) /$ $(BA \rightarrow A / I)$	$G + 2BA + H_2O \rightarrow 2A + B + 4CO_2 + 4H_2$ $G + 2BA + H_2O \rightarrow 2A + I + B + 4CO_2 + 3H_2$ $G + 2BA + H_2O \rightarrow 2I + B + 4CO_2 + 2H_2$
6. $(G \rightarrow A / I) / (BA \rightarrow B) /$ $(BA \rightarrow 2E)$	$G + 2BA \rightarrow A + B + 2E + 3CO_2$ $G + 2BA + H_2 \rightarrow 1 + B + 2E + 3CO_2$
7. $(G \rightarrow A / I) / (BA \rightarrow B) /$ $(BA \rightarrow Ac)$	$G + 2BA \rightarrow A + B + Ac + 3CO_2 + 2H_2$ $G + 2BA \rightarrow I + B + Ac + 3CO_2 + H_2$
8. $(G \rightarrow A / I) / (BA \rightarrow 2E) /$ $(BA \rightarrow A / I)$	$G + 2BA + 2H_2O \rightarrow 2A + 2E + 4CO_2 + 4H_2$ $G + 2BA + 2H_2O \rightarrow A + I + 2E + 4CO_2 + 3H_2$ $G + 2BA + 2H_2O \rightarrow 2I + 2E + 4CO_2 + 2H_2$
9. $(G \rightarrow A / I) / (BA \rightarrow A / I) /$ $(BA \rightarrow Ac)$	$G + 2BA + 2H_2O \rightarrow 2A + Ac + 4CO_2 + 6H_2$ $G + 2BA + 2H_2O \rightarrow A + I + Ac + 4CO_2 + 5H_2$ $G + 2BA + 2H_2O \rightarrow 2I + Ac + 4CO_2 + 4H_2$
10. $(G \rightarrow A / I) / (BA \rightarrow 2E) /$ $(BA \rightarrow Ac)$	$G + 2BA + H_2O \rightarrow A + 2E + Ac + 3CO_2 + 2H_2$ $G + 2BA + H_2O \rightarrow 1 + 2E + Ac + 3CO_2 + 2H_2$
11. $(G \rightarrow A / I) / (BA \rightarrow B) /$ $(BA \rightarrow A / I) / (BA \rightarrow 2E)$	$G + 3BA + H_2O \rightarrow 2A + B + 2E + 4CO_2 + 2H_2$ $G + 3BA + H_2O \rightarrow A + I + B + 2E + 4CO_2 + 2H_2$ $G + 3BA + H_2O \rightarrow 2I + B + 2E + 4CO_2$
12. $(G \rightarrow A / I) / (BA \rightarrow B) /$ $(BA \rightarrow A / I) / (BA \rightarrow Ac)$	$G + 3BA + H_2O \rightarrow 2A + B + Ac + 4CO_2 + 4H_2$ $G + 3BA + H_2O \rightarrow A + I + B + Ac + 4CO_2 + 3H_2$ $G + 3BA + H_2O \rightarrow 2I + B + Ac + 4CO_2 + 2H_2$

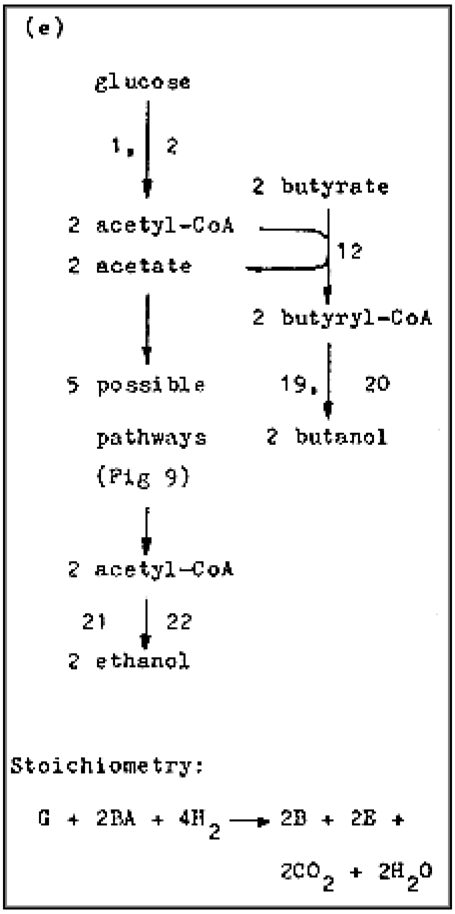
Metabolic units	Stoichiometries
13. (G $\rightarrow$ A / I) / (BA $\rightarrow$ B) / (BA $\rightarrow$ 2E) / (BA $\rightarrow$ Ac)	G + 3BA $\rightarrow$ A + B + 2E + Ac + $3CO_2$ G + 3BA + H_2 $\rightarrow$ I + B + 2E + Ac + $3CO_2$
14. (G $\rightarrow$ A / I) / (BA $\rightarrow$ A / I) / (B $\rightarrow$ 2E) / (BA $\rightarrow$ Ac)	G + 3BA + $2H_2O$ $\rightarrow$ 2A + 2E + Ac + $4CO_2$ + $4H_2$ G + 3BA + $2H_2O$ $\rightarrow$ A + I + 2E + Ac + $4CO_2$ + $3H_2$ G + 3BA + $2H_2O$ $\rightarrow$ 2I + 2E + Ac + $4CO_2$ + $2H_2$
15. (G $\rightarrow$ A / I) / (BA $\rightarrow$ B) / (BA $\rightarrow$ A / I) / (BA $\rightarrow$ 2E)	G + 4BA + H_2O $\rightarrow$ 2A + B + 2E + Ac + $4CO_2$ + $2H_2$ G + 4BA + H_2O $\rightarrow$ A + I + B + 2E + Ac + $4CO_2$ + H_2 G + 4BA + H_2O $\rightarrow$ 2I + B + 2E + Ac + $4CO_2$

Table 11. Stoichiometries of representative metabolic units resulting from the combinations of (G $\rightarrow$ 2AA) coupled with (BA $\rightarrow$ B), (BA $\rightarrow$ A / I), (BA $\rightarrow$ 2E) and (BA $\rightarrow$ Ac).

Metabolic units	Stoichiometries
1. (G $\rightarrow$ 2AA) / (BA $\rightarrow$ B)	G + BA + H_2O $\rightarrow$ 2AA + B + $2CO_2$ + $2H_2$
2. (G $\rightarrow$ 2AA) / (BA $\rightarrow$ A / I)	G + BA + $3H_2O$ $\rightarrow$ 2AA + A + $3CO_2$ + $6H_2$ G + BA + $3H_2O$ $\rightarrow$ 2AA + I + $3CO_2$ + $5H_2$
3. (G $\rightarrow$ 2AA) / (BA $\rightarrow$ 2E)	G + BA + $2H_2O$ $\rightarrow$ 2AA + 2E + $2CO_2$ + $2H_2$
4. (G $\rightarrow$ 2AA) / (BA $\rightarrow$ Ac)	G + BA + $2H_2O$ $\rightarrow$ 2AA + Ac + $2CO_2$ + $4H_2$
5. (G $\rightarrow$ 2AA) / (BA $\rightarrow$ B) / (BA $\rightarrow$ A / I)	G + 2BA + $2H_2O$ $\rightarrow$ 2AA + A + B + $3CO_2$ + $4H_2$ G + 2BA + $2H_2O$ $\rightarrow$ 2AA + I + B + $3CO_2$ + $3H_2$
6. (G $\rightarrow$ 2AA) / (BA $\rightarrow$ B) / (BA $\rightarrow$ 2E)	G + 2BA + H_2O $\rightarrow$ 2AA + B + 2E + $2CO_2$
7. (G $\rightarrow$ 2AA) / (BA $\rightarrow$ B) / (BA $\rightarrow$ Ac)	G + 2BA + H_2O $\rightarrow$ 2AA + B + Ac + $2CO_2$ + $2H_2$
8. (G $\rightarrow$ 2AA) / (BA $\rightarrow$ A / I) / (BA $\rightarrow$ 2E)	G + 2BA + $3H_2O$ $\rightarrow$ 2AA + A + 2E + $3CO_2$ + $4H_2$ G + 2BA + $3H_2O$ $\rightarrow$ 2AA + I + 2E + $3CO_2$ + $3H_2$
9. (G $\rightarrow$ 2AA) / (BA $\rightarrow$ A / I) / (BA $\rightarrow$ Ac)	G + 2BA + $3H_2O$ $\rightarrow$ 2AA + A + Ac + $3CO_2$ + $6H_2$ G + 2BA + $3H_2O$ $\rightarrow$ 2AA + I + Ac + $3CO_2$ + $5H_2$
10. (G $\rightarrow$ 2AA) / (BA $\rightarrow$ 2E) / (BA $\rightarrow$ Ac)	G + 2BA + $2H_2O$ $\rightarrow$ 2AA + 2E + Ac + $3CO_2$ + $2H_2$
11. (G $\rightarrow$ 2AA) / (BA $\rightarrow$ B) / (BA $\rightarrow$ A / I) / (BA $\rightarrow$ 2E)	G + 3BA + $2H_2O$ $\rightarrow$ 2AA + A + B + 2E + $3CO_2$ + $2H_2$ G + 3BA + $2H_2O$ $\rightarrow$ 2AA + I + B + 2E + $3CO_2$ + H_2

Metabolic units	Stoichiometries
12. (G $\longrightarrow$ 2AA) / (BA $\longrightarrow$ B) / (BA $\longrightarrow$ B) / (BA $\longrightarrow$ Ac)	G + 3BA + $2H_2O \longrightarrow$ 2AA + A + B + Ac + $3CO_2$ + $4H_2$ G + 3BA + $2H_2O \longrightarrow$ 2AA + I + B + Ac + $3CO_2$ + $3H_2$
13. (G $\longrightarrow$ 2AA) / (BA $\longrightarrow$ B) / (BA $\longrightarrow$ 2E) / (BA $\longrightarrow$ Ac)	G + 3BA + $H_2O \longrightarrow$ 2AA + B + 2E + Ac + $3CO_2$
14. (G $\longrightarrow$ 2AA) / (BA $\longrightarrow$ A / I) / (BA $\longrightarrow$ 2E) / (BA $\longrightarrow$ Ac)	G + 3BA + $3H_2O \longrightarrow$ 2AA + A + 2E + Ac + $3CO_2$ + $4H_2$ G + 3BA + $3H_2O \longrightarrow$ 2AA + I + 2E + Ac + $3CO_2$ + $3H_2$
15. (G $\longrightarrow$ 2AA) / (BA $\longrightarrow$ B) / (BA $\longrightarrow$ A / I) / (BA $\longrightarrow$ 2E) / (BA $\longrightarrow$ Ac)	G + 4BA + $2H_2O \longrightarrow$ 2AA + A + B + 2E + Ac + $3CO_2$ + $2H_2$ G + 4BA + $2H_2O \longrightarrow$ 2AA + I + B + 2E + Ac + $3CO_2$ + H_2


(a)
glucose
2NAD+
2NADH
1
2ADP
2ATP
2 pyruvate
2
2CoA
2CO2 + 2H2
2 acetyl-CoA
6
CoA
acetoacetyl-CoA
14
acetate
acetyl-CoA
acetoacetate
15
CO2
acetone
NADH
NAD+
16
isopropanol
butanol
NAD+
(NADP+)
20
NADH
(NADPH)
butyraldehyde
CoA
NAD+
19
NADH
butyryl-CoA
12
butyrate
Stoichiometry:
G + BA → A + B + 3CO2 + 2H2
G + BA → I + B + 3CO2 + H2
(b)
glucose
1, 2
6
acetoacetyl-CoA
14
acetoacetate
15,16
acetone/isopropanol
butanol
19, 20
butyryl-CoA
butyrate
Stoichiometry:
G + BA → A + B + 3CO2 + 2H2
G + BA → I + B + 3CO2 + H2
(c)
glucose
1, 2,6
7, 8,9
butyryl-CoA
12
acetate
acetyl-CoA
butyrate
7 possible
pathways
(Fig 5)
butyryl-CoA
19, 20
butanol
butanol
19, 20
butyryl-CoA
12
butyrate
Stoichiometry:
G + BA + 2H2 → 2B + 2CO2 + 2H2O
(d)
glucose
1, 2,6
7, 8,9
butyryl-CoA
12
acetoacetate
acetoacetyl-CoA
butyrate
7 possible
pathways
(Fig 5)
butyryl-CoA
19, 20
butanol
butanol
19, 20
butyryl-CoA
14
butyrate
Stoichiometry:
G + BA + 2H2 → 2B + 2CO2 + 2H2O



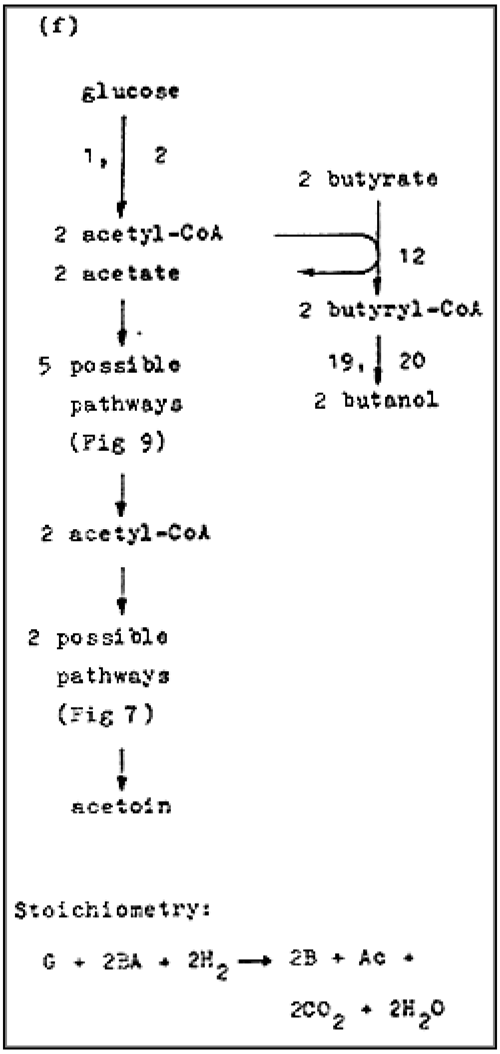


Figure 13 Metabolic units and stoichiometries of solvents formation from the co-utilization of glucose and butyric acid at solventogenesis :

(a) (G→ A / I) / (BA → B), (b) (G→ A / I) / (BA → B), (c) (G → B) / (BA → B),

(d) (G → B) / (BA → B), (e) (G → 2E) / (2BA →2B), (f) (G→ Ac) / (2BA → 2B)

III. Metabolic Units of Solvents Formation from the Co-utilization of Glucose, Acetic Acid and Butyric Acid

Metabolic units of products formation at solventogenesis, utilizing glucose, acetic acid and butyric acid as co-substrates, are analysed. Combinations of twelve or fourteen metabolic units (4 or 6 metabolic units using glucose as substrate coupled with 4 of those using acetic acid and 4 of those using butyric acid as substrates) are calculated and presented in Table 12. Some of them are determined (Table 13).

Stoichiometries corresponding to selected metabolic units are written (Table 14). Details of some metabolic units and their stoichiometries are presented in Fig. 14.

Table 12. Total numbers of metabolic units of co-substrates formed from the combinations of individual metabolic units using glucose, acetic acid or butyric acid as a substrate.

Individual metabolic units	Combinations	Total numbers of metabolic units of co-substracts Formed from the combinations of 12 metabolic units	14 metabolic units
1. (G $\rightarrow$ A / I)	3	64	96
2. (G $\rightarrow$ B)	4	288	529
3. (G $\rightarrow$ 2E)	5	560	1,448
4. (G $\rightarrow$ Ac)	6	840	2,556
5. (2AA $\rightarrow$ A / I)	7	768	3,184
6. (2AA $\rightarrow$ B)	8	492	2,912
7. (AA $\rightarrow$ E)	9	220	1,982
8. (2AA $\rightarrow$ Ac)	10	66	999
9. (BA $\rightarrow$ B)	11	12	364
10. (BA $\rightarrow$ A / I)	12	1	91
11. (BA $\rightarrow$ 2E)	13	—	14
12. (BA $\rightarrow$ Ac)	14	—	1
13. (G $\rightarrow$ 2AA)			
14. (G $\rightarrow$ BA)			
Total cases	102	3,311	14,175

Table 13. Some metabolic units of co-substrates formed from the combinations of 14 individual metabolic units using glucose or acetic acid or butyric acid as a substrate.

3 Combinations *somes of 96 cases*	*4 Combinations* *somes of 528 cases*
(G → 2AA) / (2AA → A / I) / (BA → B)	(G → 2AA) / (G → BA) / (2AA → A / I) / (BA → B)
(G → 2AA) / (2AA → A / I) / (BA → A / I)	(G → 2AA) / (G → A / I) / (AA → E) / (BA → A / I)
(G → 2AA) / (2AA → B) / (BA → B)	(G → 2AA) / (G → B) / (2AA → B) / (BA → A / I)
(G → 2AA) / (2AA → B) / (BA → B)	(G → BA) / (G → A / I) / (2AA → B) / (BA → 2E)
(G → 2AA) / (2AA → B) / (BA → A / I)	(G → BA) / (G → B) / (2AA → A / I) / (BA → 2E)
(G → 2AA) / (AA → E) / (BA → B)	(G → A / I) / (G → B) / (2AA → A / I) / (BA → B)
(G → 2AA) / (2AA → Ac) / (BA → 2E)	(G → A / I) / (G → 2E) / (2AA → B) / (BA → Ac)
(G → BA) / (2AA → A / I) / (BA → B)	(G → 2AA) / (2AA → A / I) / (2AA → B) / (BA → B)
(G → BA) / (2AA → B) / (BA → A / I)	(G → 2AA) / (2AA → A / I) / (AA → E) / (BA → A / I)
(G → BA) / (AA → E) / (BA → B)	(G → 2AA) / (2AA → B) / (AA → E) / (BA → A / I)
(G → BA) / (2AA → Ac) / (BA → A / I)	(G → BA) / (2AA → A / I) / (2AA → Ac) / (BA → 2E)
(G → A / I) / (2AA → A / I) / (BA → B)	(G → BA) / / (2AA → B) / (AA → E) / (BA → A / I)
(G → A / I) / (2AA → A / I) / (BA → 2E)	(G → A / I) / (2AA → A / I) / (2AA → B) / (BA → 2E)
(G → A / I) / (2AA → B) / (BA → A / I)	(G → A / I) / (2AA → A / I) / (AA → E) / (BA → B)
(G → A / I) / (AA → E) / (BA → B)	(G → B) / / (2AA → B) / (2AA → Ac) / (BA → A / I)
(G → A / I) / (AA → E) / (BA → Ac)	(G → 2AA) / (2AA → A / I) / (BA → B) / (BA → A / I)
(G → A / I) / (2AA → Ac) / (BA → B)	(G → 2AA) / (2AA → A / I) / (BA → B) / (BA → 2E)
(G → B) / (2AA → A / I) / (BA → A / I)	(G → 2AA) / (2AA → B) / (BA → B) / (BA → A / I)
(G → B) / (2AA → B) / (BA → B)	(G → 2AA) / (AA → E) / (BA → A / I) / (BA → Ac)
(G → B) / (AA → E) / (BA → 2E)	(G → BA) / (2AA → A / I) / (BA → B) / (BA → 2E)
(G → 2E) / (2AA → A / I) / (BA → 2E)	(G → A / I) / (2AA → A / I) / (BA → B) / (BA → A / I)
(G → Ac) / (2AA → B) / (BA → A / I)	(G → B) / (2AA → Ac) / (BA → A / I) / (BA → 2E)

5 Combinations   *somes of 1448 cases*
(G → 2AA) / (G → BA) / (G → A / I) / (2AA → A / I) / (BA → B)
(G → 2AA) / (G → BA) / (G → B) / (2AA → B) / (BA → A / I)
(G → 2AA) / (G → A / I) / (G → B) / (AA → E) / (BA → Ac)
(G → 2AA) / (G → A / I) / (G → 2E) / (2AA → A / I) / (BA → B)
(G → 2AA) / (G → B) / (G → 2E) / (2AA → Ac) / (BA → A / I)
(G → BA) / (G → A / I) / (G → B) / (AA → E) / (BA → B)
(G → BA) / (G → A / I) / (G → 2E) / (2AA → B) / (BA → B)
(G → BA) / (G → B) / (G → 2E) / (2AA → A / I) / (BA → B)
(G → A / I) / (G → B) / (G → 2E) / (2AA → B) / (BA → A / I)
(G → 2AA) / (G → BA) / (2AA → A / I) / (2AA → B) / (BA → B)
(G → 2AA) / (G → A / I) / (AA → E) / (2AA → Ac) / (BA → B)
(G → 2AA) / (G → B) / (2AA → A / I) / (2AA → B) / (BA → 2E)
(G → BA) / (G → A / I) / (2AA → B) / (AA → E) / (BA → B)
(G → BA) / (G → B) / (2AA → A / I) / (AA → E) / (BA → Ac)
(G → A / I) / (G → B) / (2AA → A / I) / (2AA → B) / (BA → B)
(G → A / I) / (G → 2E) / (2AA → B) / (2AA → Ac) / (BA → B)
(G → 2AA) / (G → BA) / (2AA → A / I) / (BA → B) / (BA → A / I)
(G → 2AA) / (G → A / I) / (2AA → B) / (BA → A / I) / (BA → 2E)
(G → 2AA) / (G → B) / (AA → E) / (BA → B) / (BA → A / I)
(G → BA) / (G → A / I) / (2AA → Ac) / (BA → B) / (BA → 2E)
(G → BA) / (G → B) / (2AA → A / I) / (BA → B) / (BA → Ac)
(G → A / I) / (G → 2E) / (2AA → B) / (BA → A / I) / (BA → B)
(G → A / I) / (G → Ac) / (2AA → B) / (BA → B) / (BA → 2E)
(G → 2AA) / (2AA → A / I) / (2AA → B) / (AA → E) / (BA → B)
(G → BA) / (2AA → B) / (AA → E) / (2AA → Ac) / (BA → A / I)
(G → A / I) / (2AA → A / I) / (2AA → B) / (AA → E) / (BA → B)
(G → 2AA) / (2AA → A / I) / (2AA → B) / (BA → B) / (BA → 2E)
(G → BA) / (2AA → B) / (AA → E) / (BA → B) / (BA → A / I)
(G → A / I) / (2AA → B) / (2AA → Ac) / (BA → A / I) / (BA → 2E)
(G → 2AA) / (2AA → A / I) / (BA → B) / (BA → A / I) / (BA → 2E)
(G → BA) / (2AA → B) / (BA → A / I) / (BA → 2E) / (BA → Ac)
(G → A / I) / (AA → E) / (BA → B) / (BA → A / I) / (BA → 2E)

6 Combinations *somes of 2556 cases*
(G → 2AA) / (G → BA) / (G → A / I) / (G → B) / (2AA → A / I) / (BA → B)
(G → 2AA) / (G → A / I) / (G → B) / (G → 2E) / (2AA → B) / (BA → A / I)
(G → BA) / (G → A / I) / (G → 2E) / (G → Ac) / (AA → E) / (BA → B)
(G → A / I) / (G → B) / (G → 2E) / (G → Ac) / (2AA → A / I) / (BA → B)
(G → 2AA) / (G → BA) / (G → A / I) / (2AA → A / I) / (2AA → B) / (BA → 2E)
(G → 2AA) / (G → A / I) / (G → B) / (2AA → B) / (AA → E) / (BA → B)
(G → A / I) / (G → B) / (G → 2E) / (2AA → A / I) / (2AA → Ac) / (BA → A / I)
(G → BA) / (G → A / I) / (G → B) / (2AA → B) / (AA → E) / (BA → B)
(G → A / I) / (G → B) / (G → 2E) / (AA → E) / (2AA → Ac) / (BA → B)
(G → 2AA) / (G → BA) / (G → A / I) / (2AA → A / I) / (BA → A / I) / (BA → B)
(G → 2AA) / (G → BA) / (G → 2E) / (2AA → B) / (BA → B) / (BA → A / I)
(G → BA) / (G → A / I) / (G → B) / (AA → E) / (BA → B) / (BA → Ac)
(G → A / I) / (G → B) / (G → Ac) / (2AA → A / I) / (BA → B) / (BA → 2E)
(G → B) / (G → 2E) / (G → Ac) / (2AA → A / I) / (BA → B) / (BA → A / I)
(G → 2AA) / (G → BA) / (2AA → A / I) / (2AA → B) / (AA → E) / (BA → B)
(G → A / I) / (G → B) / (2AA → A / I) / (2AA → B) / (2AA → Ac) / (BA → 2E)
(G → 2E) / (G → Ac) / (2AA → A / I) / (AA → E) / (2AA → Ac) / (BA → B)
(G → 2AA) / (G → BA) / (2AA → A / I) / (2AA → B) / (BA → B) / (BA → 2E)
(G → 2AA) / (G → A / I) / (2AA → B) / (AA → E) / (BA → B) / (BA → A / I)
(G → BA) / (G → A / I) / (AA → E) / (2AA → Ac) / (BA → B) / (BA → A / I)
(G → A / I) / (G → 2E) / (2AA → A / I) / (2AA → B) / (BA → 2E) / (BA → Ac)
(G → 2AA) / (G → BA) / (2AA → A / I) / (BA → B) / (BA → A / I) / (BA → 2E)
(G → BA) / (G → A / I) / (2AA → B) / (BA → A / I) / (BA → 2E) / (BA → Ac)
(G → A / I) / (G → B) / (AA → E) / (BA → B) / (BA → A / I) / (BA → 2E)
(G → B) / (G → 2E) / (2AA → B) / (BA → B) / (BA → 2E) / (BA → Ac)
(G → 2AA) / (2AA → A / I) / (2AA → B) / (AA → E) / (2AA → Ac) / (BA → B)
(G → A / I) / (2AA → A / I) / (2AA → B) / (AA → E) / (2AA → Ac) / (BA → A / I)
(G → 2AA) / (2AA → A / I) / (2AA → B) / (AA → E) / (BA → B) / (BA → 2E)
(G → BA) / (2AA → A / I) / (AA → E) / (2AA → Ac) / (BA → 2E) / (BA → Ac)
(G → 2AA) / (2AA → A / I) / (2AA → B) / (BA → B) / (BA → A / I) / (BA → 2E)
(G → A / I) / (AA → E) / (2AA → Ac) / (BA → B) / (BA → 2E) / (BA → Ac)
(G → 2AA) / (2AA → A / I) / (BA → B) / (BA → A / I) / (BA → 2E) / (BA → Ac)
(G → A / I) / (AA → E) / (BA → B) / (BA → A / I) / (BA → 2E) / (BA → Ac)

7 Combinations   *somes of 3184 cases*
(G → 2AA) / (G → BA) / (G → A / I) / (G → B) / (G → 2E) / (2AA → A / I) / (BA → B)
(G → BA) / (G → A / I) / (G → B) / (G → 2E) / (G → Ac) / (2AA → B) / (BA → A / I)
(G → 2AA) / (G → BA) / (G → A / I) / (G → B) / (2AA → A / I) / (AA → E) / (BA → B)
(G → BA) / (G → A / I) / (G → B) / (G → 2E) / (2AA → A / I) / (2AA → B) / (BA → A / I)
(G → A / I) / (G → B) / (G → 2E) / (G → Ac) / (AA → E) / (2AA → Ac) / (BA → B)
(G → 2AA) / (G → BA) / (G → A / I) / (G → 2E) / (2AA → A / I) / (BA → B) / (BA → A / I)
(G → 2AA) / (G → A / I) / (G → B) / (G → 2E) / (AA → E) / (BA → A / I) / (BA → 2E)
(G → BA) / (G → A / I) / (G → B) / (G → Ac) / (2AA → B) / (BA → B) / (BA → A / I)
(G → 2AA) / (G → BA) / (G → A / I) / (2AA → A / I) / (2AA → B) / (AA → E) / (BA → B)
(G → BA) / (G → A / I) / (G → 2E) / (2AA → B) / (AA → E) / (2AA → Ac) / (BA → B)
(G → A / I) / (G → B) / (G → Ac) / (2AA → A / I) / (AA → E) / (2AA → Ac) / (BA → 2E)
(G → 2AA) / (G → A / I) / (G → B) / (2AA → A / I) / (2AA → B) / (BA → B) / (BA → A / I)
(G → 2AA) / (G → B) / (G → 2E) / (2AA → A / I) / (AA → E) / (BA → A / I) / (BA → 2E)
(G → BA) / (G → A / I) / (G → B) / (AA → E) / (2AA → Ac) / (BA → B) / (BA → Ac)
(G → 2AA) / (G → BA) / (G → A / I) / (2AA → A / I) / (BA → B) / (BA → A / I) / (BA → 2E)
(G → 2AA) / (G → B) / (G → 2E) / (2AA → B) / (BA → A / I) / (BA → 2E) / (BA → Ac)
(G → A / I) / (G → B) / (G → 2E) / (AA → E) / (BA → B) / (BA → 2E) / (BA → Ac)
(G → 2AA) / (G → BA) / (2AA → A / I) / (2AA → B) / (AA → E) / (2AA → Ac) / (BA → B)
(G → BA) / (G → A / I) / (2AA → A / I) / (2AA → B) / (AA → E) / (2AA → Ac) / (BA → A / I)
(G → A / I) / (G → B) / (2AA → A / I) / (2AA → B) / (AA → E) / (2AA → Ac) / (BA → 2E)
(G → 2AA) / (G → A / I) / (2AA → A / I) / (2AA → B) / (AA → E) / (BA → B) / (BA → A / I)
(G → BA) / (G → A / I) / (2AA → B) / (AA → E) / (2AA → Ac) / (BA → B) / (BA → 2E)
(G → A / I) / (G → B) / (2AA → B) / (2AA → A / I) / (AA → E) / (BA → 2E) / (BA → Ac)
(G → 2AA) / (G → BA) / (2AA → A / I) / (2AA → B) / (BA → B) / (BA → A / I) / (BA → 2E)
(G → BA) / (G → A / I) / (2AA → B) / (AA → E) / (BA → A / I) / (BA → 2E) / (BA → Ac)
(G → A / I) / (G → B) / (2AA → A / I) / (2AA → B) / (BA → B) / (BA → A / I) / (BA → 2E)
(G → 2AA) / (G → BA) / (2AA → A / I) / (BA → B) / (BA → A / I) / (BA → 2E) / (BA → Ac)
(G → BA) / (G → A / I) / (2AA → B) / (BA → B) / (BA → A / I) / (BA → 2E) / (BA → Ac)
(G → 2AA) / (2AA → A / I) / (2AA → B) / (AA → E) / (2AA → Ac) / (BA → B) / (BA → A / I)
(G → A / I) / (2AA → A / I) / (2AA → B) / (AA → E) / (2AA → Ac) / (BA → A / I) / (BA → 2E)
(G → 2AA) / (2AA → A / I) / (2AA → B) / (AA → E) / (BA → B) / (BA → A / I) / (BA → 2E)
(G → A / I) / (2AA → B) / (AA → E) / (2AA → Ac) / (BA → A / I) / (BA → 2E) / (BA → Ac)
(G → 2AA) / (2AA → A / I) / (2AA → B) / (BA → B) / (BA → A / I) / (BA → 2E) / (BA → Ac)
(G → A / I) / (2AA → B) / (AA → E) / (BA → B) / (BA → A / I) / (BA → 2E) / (BA → Ac)

8 Combinations   *somes of 2912 cases*
(G → 2AA) / (G → BA) / (G → A / I) / (G → B) / (G → 2E) / (G → Ac) / (2AA → A / I) / (BA → B)
(G → 2AA) / (G → BA) / (G → A / I) / (G → B) / (G → 2E) / (G → Ac) / (2AA → B) / (BA → A / I)
(G → 2AA) / (G → BA) / (G → A / I) / (G → B) / (G → 2E) / (2AA → A / I) / (2AA → B) / (BA → B)
(G → BA) / (G → A / I) / (G → B) / (G → 2E) / (G → Ac) / (2AA → A / I) / (AA → E) / (BA → B)
(G → 2AA) / (G → BA) / (G → A / I) / (G → 2E) / (G → Ac) / (AA → E) / (BA → B) / (BA → A / I)
(G → 2AA) / (G → A / I) / (G → B) / (G → 2E) / (G → Ac) / (2AA → B) / (BA → B) / (BA → 2E)
(G → 2AA) / (G → BA) / (G → A / I) / (G → B) / (2AA → A / I) / (2AA → B) / (AA → E) / (BA → B)
(G → A / I) / (G → B) / (G → 2E) / (G → Ac) / (2AA → A / I) / (AA → E) / (2AA → Ac) / (BA → A / I)
(G → 2AA) / (G → BA) / (G → B) / (G → 2E) / (2AA → A / I) / (2AA → B) / (BA → B) / (BA → A / I)
(G → BA) / (G → A / I) / (G → B) / (G → 2E) / (AA → E) / (2AA → Ac) / (BA → A / I) / (BA → 2E)
(G → 2AA) / (G → BA) / (G → A / I) / (G → B) / (2AA → A / I) / (BA → B) / (BA → A / I) / (BA → 2E)
(G → BA) / (G → A / I) / (G → B) / (G → 2E) / (AA → E) / (BA → B) / (BA → 2E) / (BA → Ac)
(G → 2AA) / (G → BA) / (G → A / I) / (2AA → A / I) / (2AA → B) / (AA → E) / (2AA → Ac) / (BA → B)
(G → 2AA) / (G → A / I) / (G → B) / (2AA → A / I) / (2AA → B) / (AA → E) / (2AA → Ac) / (BA → A / I)
(G → 2AA) / (G → BA) / (G → B) / (2AA → A / I) / (2AA → B) / (AA → E) / (BA → B) / (BA → 2E)
(G → BA) / (G → A / I) / (G → B) / (2AA → B) / (AA → E) / (2AA → Ac) / (BA → B) / (BA → Ac)
(G → 2AA) / (G → BA) / (G → 2E) / (2AA → A / I) / (AA → E) / (BA → B) / (BA → A / I) / (BA → 2E)
(G → A / I) / (G → B) / (G → 2E) / (2AA → A / I) / (2AA → B) / (BA → B) / (BA → 2E) / (BA → Ac)
(G → 2AA) / (G → BA) / (G → A / I) / (2AA → A / I) / (BA → B) / (BA → A / I) / (BA → 2E) / (BA → Ac)
(G → BA) / (G → A / I) / (G → B) / (2AA → B) / (BA → B) / (BA → A / I) / (BA → 2E) / (BA → Ac)
(G → 2AA) / (G → BA) / (2AA → A / I) / (2AA → B) / (AA → E) / (2AA → Ac) / (BA → B) / (BA → A / I)
(G → A / I) / (G → B) / (2AA → A / I) / (2AA → B) / (AA → E) / (2AA → Ac) / (BA → B) / (BA → 2E)
(G → 2AA) / (G → BA) / (2AA → A / I) / (2AA → B) / (AA → E) / (BA → B) / (BA → A / I) / (BA → 2E)
(G → BA) / (G → A / I) / (2AA → A / I) / (AA → E) / (2AA → Ac) / (BA → B) / (BA → 2E) / (BA → Ac)
(G → 2AA) / (G → A / I) / (2AA → A / I) / (2AA → B) / (BA → B) / (BA → A / I) / (BA → 2E) / (BA → Ac)
(G → 2AA) / (G → B) / (2AA → A / I) / (AA → E) / (BA → B) / (BA → A / I) / (BA → 2E) / (BA → Ac)
(G → 2AA) / (2AA → A / I) / (2AA → B) / (AA → E) / (2AA → Ac) / (BA → B) / (BA → A / I) / (BA → 2E)
(G → A / I) / (2AA → A / I) / (2AA → B) / (AA → E) / (2AA → Ac) / (BA → B) / (BA → 2E) / (BA → Ac)
(G → 2AA) / (2AA → A / I) / (2AA → B) / (AA → E) / (BA → B) / (BA → A / I) / (BA → 2E) / (BA → Ac)
(G → A / I) / (2AA → B) / (AA → E) / (2AA → Ac) / (BA → B) / (BA → A / I) / (BA → 2E) / (BA → Ac)

9 Combinations ——————— *somes of 1982 cases*
(G → 2AA) / (G → BA) / (G → A / I) / (G → B) / (G → 2E) / (G → Ac) / (2AA → A / I) / (2AA → B) / (BA → B)
(G → 2AA) / (G → BA) / (G → A / I) / (G → B) / (G → 2E) / (G → Ac) / (2AA → A / I) / (AA → E) / (BA → A / I)
(G → 2AA) / (G → BA) / (G → A / I) / (G → B) / (G → 2E) / (G → Ac) / (2AA → A / I) / (BA → B) / (BA → A / I)
(G → 2AA) / (G → BA) / (G → A / I) / (G → B) / (G → 2E) / (G → Ac) / (2AA → B) / (BA → B) / (BA → 2E)
(G → 2AA) / (G → BA) / (G → A / I) / (G → B) / (G → 2E) / (2AA → A / I) / (2AA → B) / (AA → E) / (BA → B)
(G → BA) / (G → A / I) / (G → B) / (G → 2E) / (G → Ac) / (2AA → A / I) / (2AA → B) / (AA → E) / (BA → A / I)
(G → 2AA) / (G → BA) / (G → B) / (G → 2E) / (G → Ac) / (2AA → A / I) / (2AA → B) / (BA → B) / (BA → A / I)
(G → 2AA) / (G → A / I) / (G → B) / (G → 2E) / (G → Ac) / (2AA → B) / (AA → E) / (BA → B) / (BA → 2E)
(G → 2AA) / (G → BA) / (G → A / I) / (G → B) / (G → 2E) / (2AA → A / I) / (BA → B) / (BA → A / I) / (BA → 2E)
(G → 2AA) / (G → A / I) / (G → B) / (G → 2E) / (G → Ac) / (AA → E) / (BA → A / I) / (BA → 2E) / (BA → Ac)
(G → 2AA) / (G → BA) / (G → A / I) / (G → B) / (2AA → A / I) / (2AA → B) / (AA → E) / (2AA → Ac) / (BA → B)
(G → 2AA) / (G → A / I) / (G → B) / (G → 2E) / (2AA → A / I) / (2AA → B) / (AA → E) / (2AA → Ac) / (BA → A / I)
(G → BA) / (G → A / I) / (G → B) / (G → 2E) / (2AA → A / I) / (2AA → B) / (AA → E) / (BA → B) / (BA → A / I)
(G → A / I) / (G → B) / (G → 2E) / (G → Ac) / (2AA → A / I) / (2AA → B) / (AA → E) / (BA → B) / (BA → 2E)
(G → 2AA) / (G → BA) / (G → A / I) / (G → B) / (2AA → A / I) / (2AA → B) / (BA → B) / (BA → A / I) / (BA → 2E)
(G → 2AA) / (G → A / I) / (G → B) / (G → 2E) / (2AA → B) / (AA → E) / (BA → A / I) / (BA → 2E) / (BA → Ac)
(G → 2AA) / (G → BA) / (G → A / I) / (G → B) / (2AA → A / I) / (BA → B) / (BA → A / I) / (BA → 2E) / (BA → Ac)
(G → BA) / (G → A / I) / (G → B) / (G → 2E) / (2AA → B) / (BA → B) / (BA → A / I) / (BA → 2E) / (BA → Ac)
(G → 2AA) / (G → BA) / (G → A / I) / (2AA → A / I) / (2AA → B) / (AA → E) / (2AA → Ac) / (BA → B) / (BA → A / I)
(G → A / I) / (G → B) / (G → 2E) / (2AA → A / I) / (2AA → B) / (AA → E) / (2AA → Ac) / (BA → B) / (BA → 2E)
(G → 2AA) / (G → BA) / (G → B) / (2AA → A / I) / (2AA → B) / (AA → E) / (BA → B) / (BA → A / I) / (BA → 2E)
(G → BA) / (G → A / I) / (G → B) / (2AA → A / I) / (AA → E) / (2AA → Ac) / (BA → B) / (BA → A / I) / (BA → Ac)
(G → 2AA) / (G → A / I) / (G → 2E) / (2AA → A / I) / (2AA → B) / (BA → B) / (BA → A / I) / (BA → 2E) / (BA → Ac)
(G → 2AA) / (G → BA) / (2AA → A / I) / (2AA → B) / (AA → E) / (2AA → Ac) / (BA → B) / (BA → A / I) / (BA → 2E)
(G → A / I) / (G → B) / (2AA → A / I) / (2AA → B) / (AA → E) / (2AA → Ac) / (BA → B) / (BA → 2E) / (BA → Ac)
(G → 2AA) / (G → A / I) / (2AA → A / I) / (2AA → B) / (AA → E) / (BA → B) / (BA → A / I) / (BA → 2E) / (BA → Ac)
(G → BA) / (G → A / I) / (2AA → B) / (AA → E) / (2AA → Ac) / (BA → B) / (BA → A / I) / (BA → 2E) / (BA → Ac)
(G → 2AA) / (2AA → A / I) / (2AA → B) / (AA → E) / (2AA → Ac) / (BA → B) / (BA → A / I) / (BA → 2E) / (BA → Ac)
(G → A / I) / (2AA → A / I) / (2AA → B) / (AA → E) / (2AA → Ac) / (BA → B) / (BA → A / I) / (BA → 2E) / (BA → Ac)

Table 14. Stoichiometries of representative metabolic units of co-substrates formed from the combinations of individual metabolic units using glucose, acetic acid or butyric acid as a substrate.

Metabolic units	Stoichiometries
1. (G → 2AA) / (2AA → A / I) / (BA → B)	G + BA → A + B + $3CO_2$ + $2H_2$ G + BA → I + B + $3CO_2$ + H_2
2. (G → 2AA) / (2AA → B) / (BA → A / I)	G + BA → A + B + $2CO_2$ + $2H_2$ G + BA → I + B + $2CO_2$ + H_2
3. (G → BA) / (2AA → A / I) / (BA → B)	G + 2AA → A + B + $3CO_2$ + $2H_2O$ G + 2AA + H_2 → I + B + 3 CO_2 + $2H_2O$
4. (G → BA) / (2AA → B) / (BA → A / I)	G + 2AA → A + B + $3CO_2$ + $2H_2O$ G + 2AA + H_2 → I + B + $3CO_2$ + $2H_2O$ G + 2AA + BA → A + I + B + $4CO_2$ + H_2 + H_2O
5. (G → 2AA) / (G → BA) / (2AA → A / I) / (BA → B)	2G → A + B + $5CO_2$ + 4 H_2 2G + 2AA → A + I + B + $6CO_2$ + $3H_2$ + H_2O 2G → I + B + $5CO_2$ + $3H_2$
6. (G → 2AA) / (G → A / I) / (2AA → A / I) / (2AA → B) / (BA → B)	2G + 2AA + BA → 2A + 2B + $6CO_2$ + $2H_2O$ + $2H_2$ 2G + 2AA + BA → A + I + 2B + $6CO_2$ + $2H_2O$ + H_2 2G + 2AA + BA → 2I + 2B + $6CO_2$ + $2H_2O$
7. (G → 2AA) / (G → BA) / (G → A / I) / (2AA → A / I) / (AA → E) / (BA → B)	3G + AA → 2A + B + E + $8CO_2$ + 6 H_2 3G + AA → A + I + B + E + $8CO_2$ + 5 H_2 3G + AA → 2I + B + E + $8CO_2$ + 4 H_2
8. (G → 2AA) / (G → BA) / (G → A / I) / (G → B) / (2AA → A / I) / (BA → B) / (BA → A / I)	4G + BA + H_2O → 3A + 2B + $11CO_2$ + $10H_2$ 4G + BA + H_2O → 2A + I + 2B + $11CO_2$ + $9H_2$ 4G + BA + H_2O → 2I + A + 2B + $11CO_2$ + $8H_2$ 4G + 2AA + BA → 3A + I + 2B + $12CO_2$ + 11 H_2 4G + 2AA + BA + H_2O → 2A + 2I + 2B + $12CO_2$ + 8 H_2 4G + 2BA + $2H_2O$ → 3A + I + 2B + $12CO_2$ + $11H_2$
9. (G → 2AA) / (G → BA) / (G → A / I) / (G → 2E) / (2AA → A / I) / (2AA → B) / (BA → B) / (BA → A / I)	4G + 2AA + BA → 3A + 2B + 2E + $11CO_2$ + $6H_2$ + H_2O 4G + 2AA + BA → 2A + I + 2B + 2E + $11CO_2$ + $5H_2$ + H_2O 4G + 2AA + BA → A + 2I + 2B + 2E + $11CO_2$ + $4H_2$ 4G + 2AA + 2BA + H_2O → A + 3I + 2B + 2E + $12CO_2$ + $5H_2$

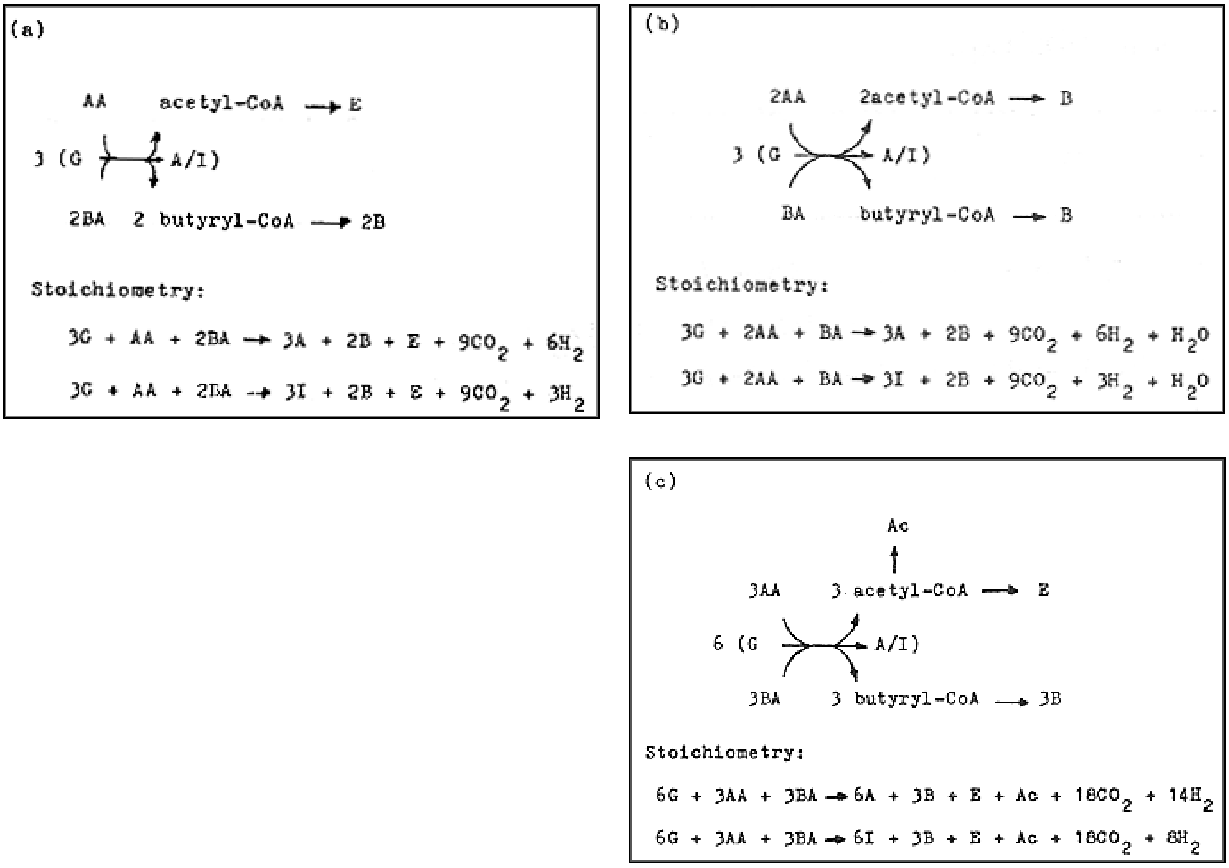


Figure 14 Metabolic units and stoichiometries of solvents formation from the co-utilization of glucose, acetic acid and butyric acid at solventogenesis :

(a) 3 (G→ A / 1) / (AA → E) / 2 (BA→ B), (b) 3 (G→ A / I) / (2AA →B) / (BA→B),

(b) 6 (G→ A / I) / (AA→E) / (2AA → Ac) / 3 (BA→ B)

3. PROPOSED BIOCHEMICAL PATHWAYS BASED ON THE AUTHOR'S STOICHIOMETRIES FOR EXPERIMENTAL DATA FROM VARIOUS RESEARCHERS

Experimental data of ABE/IBE fermentations from literatures are used to demonstrate the author's approach for writing stoichiometries and corresponding biochemical pathways.

Example 1 Fermentation of glucose with **C. butylicum ;** data were from Klyuer 1931 : glucose fermented was 100 moles, carbon recovery (as glucose) was 97 moles ; products formed (moles) were AA 42.7, BA 75.4, H_2 231, CO_2 196 and CO_2 consistency test 193.5/196.

The proposed biochemical pathways based on the author's stoichiometry for these data are shown in Fig. 15.

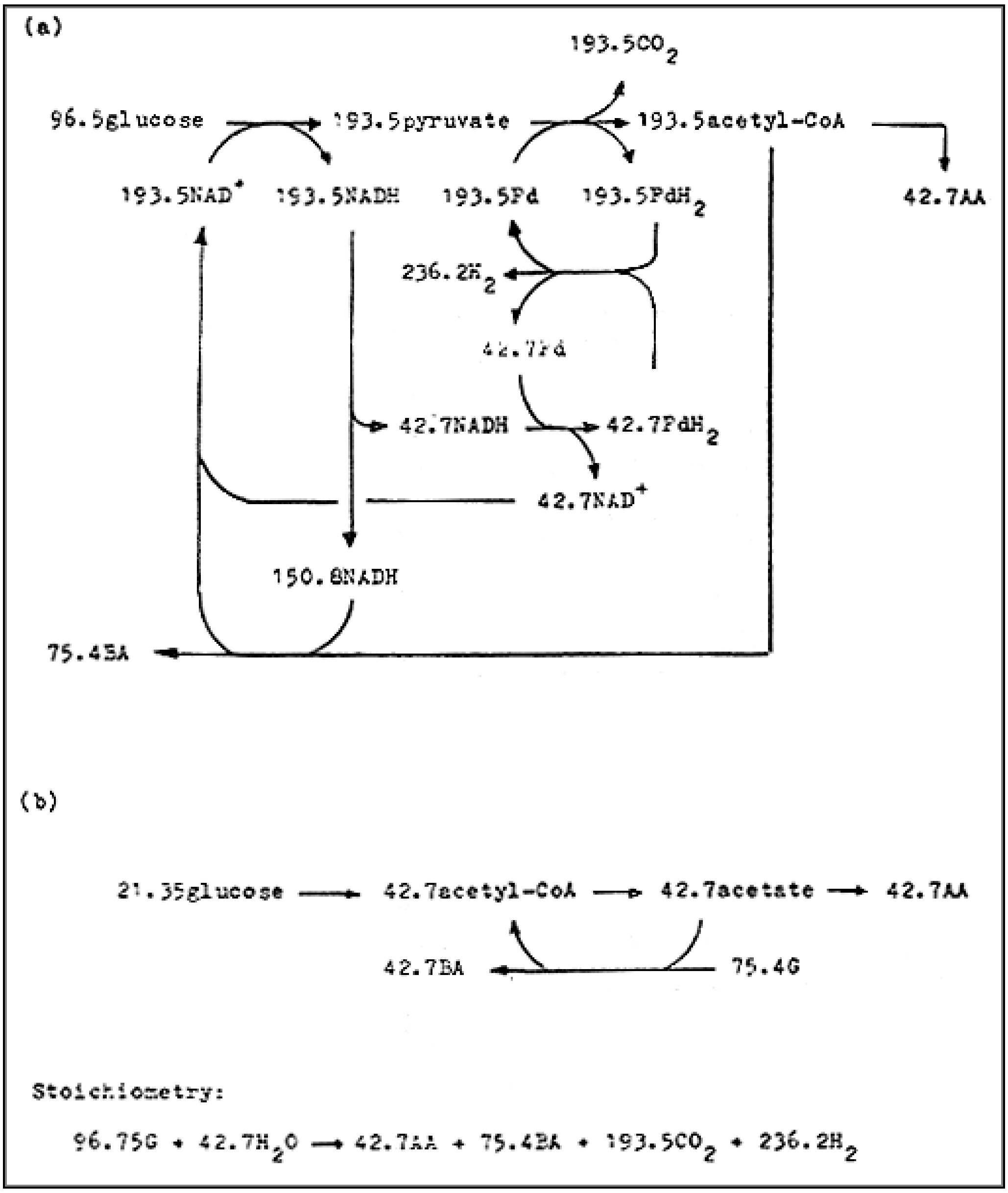
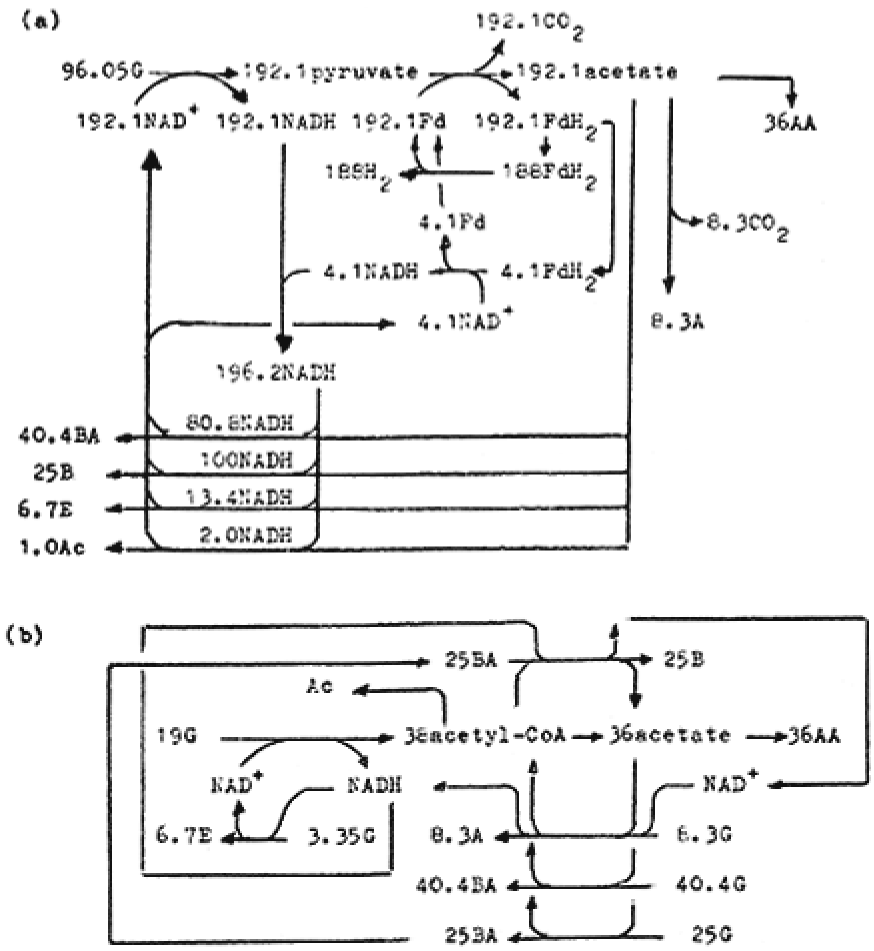


Figure 15 The author's stoichiometry and proposed biochemical pathways for experimental data from Kluyer 1931 : (a) showing material balance, (b) showing acetate/acetyl-CoA loop.

Example 2 Fermentation of glucose with **C. falsineum** ; data were from van der Lek 1930 : glucose fermented was 100 moles, carbon recovery (as glucose) was 97.3 moles ; products formed (moles) were AA 36.0, BA 40.4, A 8.3, B 25.0, E 6.7, Ac 1.0, H_2 186.0, CO_2 208.0 and CO_2 consistency test 200/208.

The proposed biochemical pathways based on the author's stoichiometry for these data are shown in Fig. 16.



Stoichiometry:

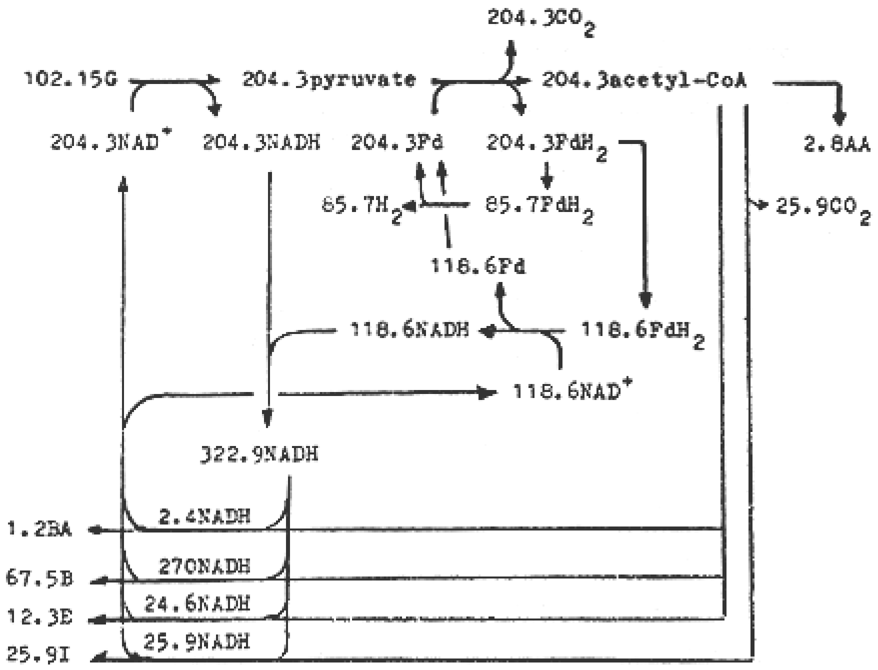
$$96.05G + 19.30H_2O \longrightarrow 36.0AA + 40.4BA + 8.3A + 25.0B + 6.7E + 1.0Ac + 200.4CO_2 + 188.0H_2$$

Figure 16 The author's stoichiometry and proposed biochemical pathways for experimental data from van der Lek 1930 :

(a) showing material balance, (b) showing acetate/acetyl-CoA loop.

Example 3 Fermentation of glucose with **C. butylicum** ; data were from van der Lek 1930 : glucose fermented was 100 moles, glucose recovery was 100.5 moles ; products formed (moles) were AA 2.8, BA 1.2, I 25.9, B 67.5, E 12.3, H_2 81.2, CO_2 220 and CO_2 consistency test 220/230.

The proposed biochemical pathways based on the author's stoichiometry for these data are shown in Fig. 17.



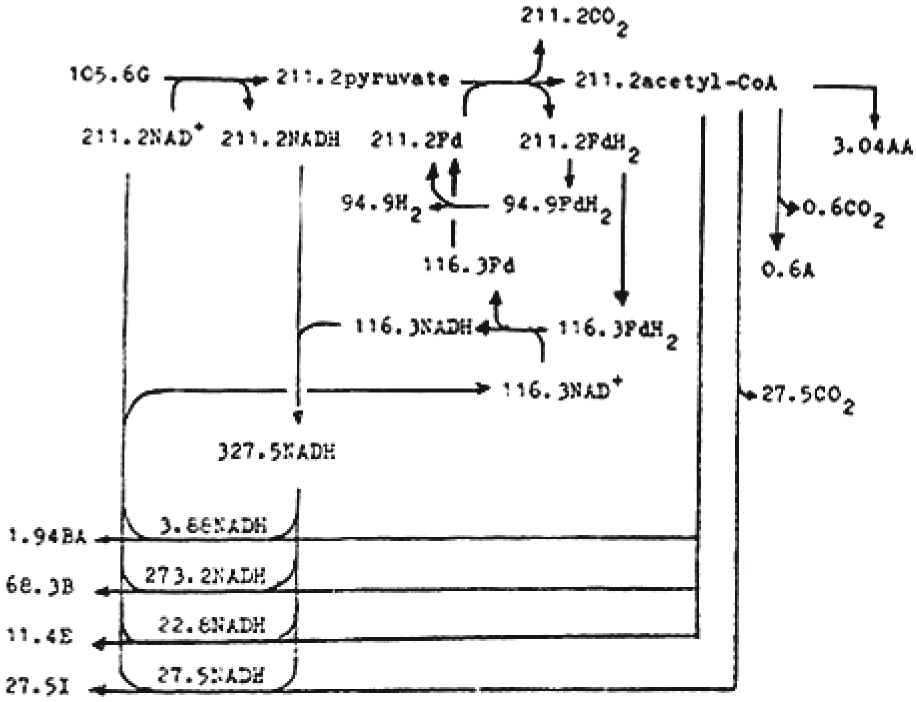
Stoichiometry:

$$102.15G \rightarrow 2.8AA + 1.2BA + 25.9I + 67.5B + 12.3E + 230.2CO_2 + $$
$$+ 85.7H_2 + 38.8H_2O$$

Figure 17 The author's stoichiometry and proposed biochemical pathways for experimental data from van der Lek 1930 : showing material balance.

Example 4 Fermentation of glucose with **C. butylicum** ; data were from van der Lek 1930 : glucose fermented was 100 moles, glucose recovery was 103 moles ; products formed (moles) were AA 3.04, BA 1.94, A 0.6, I 27.5, B 68.3, E 11.4, H_2 95.0, CO_2 224.5 and CO_2 consistency test 224.5 / 239.

The proposed biochemical pathways based on the author's stoichiometry for these data are shown in Fig. 18.



Stoichiometry:

$$105.6G \rightarrow 3.04AA + 1.94BA + 0.6A + 27.5I + 68.3B + 11.4E + 239.3CO_2 + 94.9H_2 + 37.2H_2O$$

Figure 18 The author's stoichiometry and proposed biochemical pathways for experimental data from van der Lek 1930 : showing material balance.

Exaxnple 5 Batch fermentation of glucose with **C. acetobutylicum** ATCC 824 ; data were from Leung and Wang 1981 : glucose fermented was 65 g / l ; products formed (g / l) were BA 3.5, A 7.0, B 12.0, E 1.5 and biomass 3.5.

The proposed biochemical pathways based on the author's stoichiometry for these data are shown in Fig. 19.

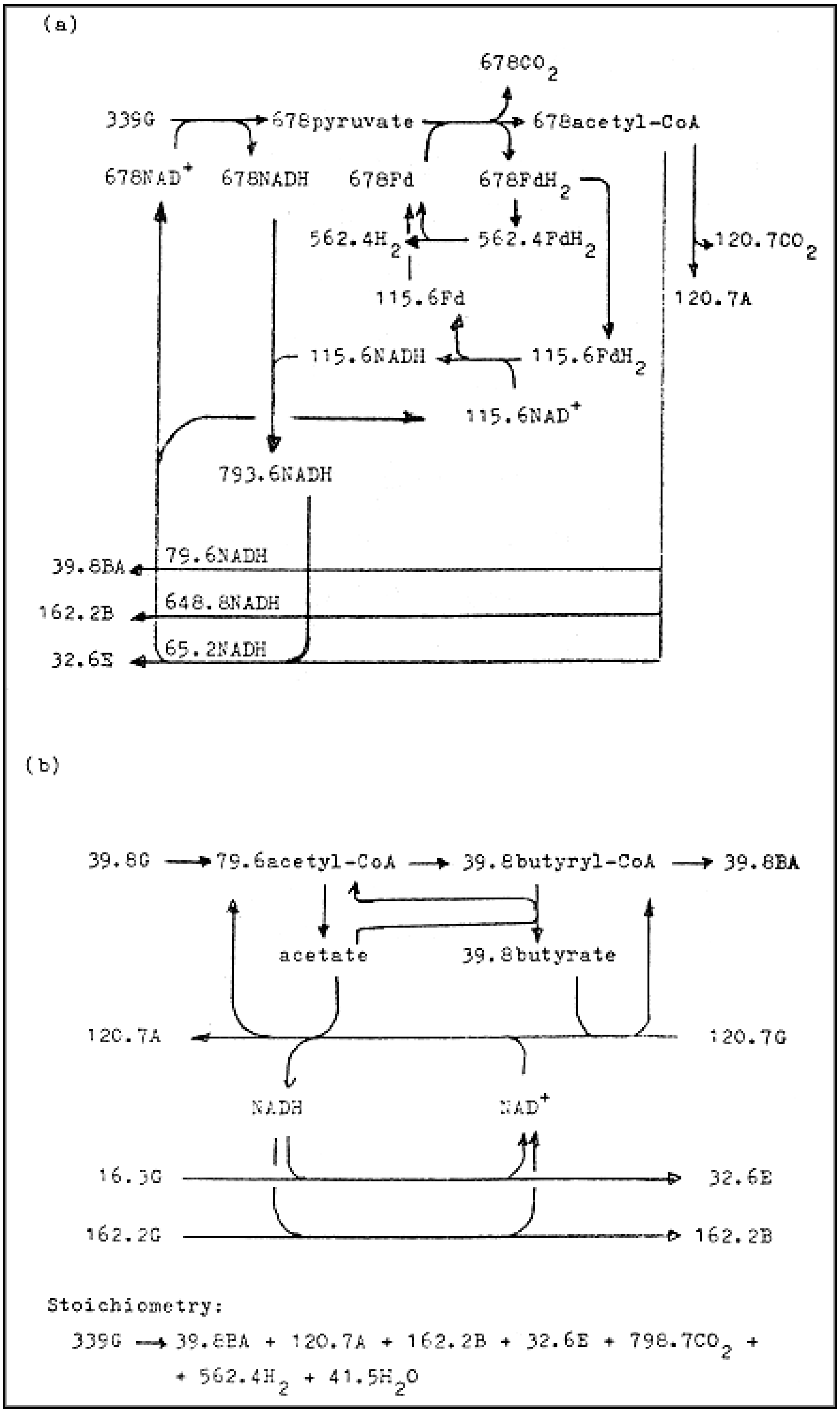


Figure 19 The author's stoichiometry and proposed biochemical pathways for experimental data from Leung and Wang 1981 :

(a) showing material balance, (b) showing acetate/acetyl-CoA loop.

Example 6 Fermentation of glucose (2%) by **C. acetobutylicum** NCIB 8052 without and with organic acids addition ; data were from Holt et al 1984 :

Without organic acid addition, products formed (mM) were AA 34, BA 16, A 22, B 51 and E 2 ;

With 20 mM acetic acid addition, products formed (mM) were AA 22, BA 5, A 25, B 20 and E 3 ;

With 20 mM butyric acid addition, products formed (mM) were AA 38, BA 20, A 25, B 53 and E 3 ;

With 10 mM acetic acid plus 10 mM butyric acid addition, products formed (mM) were AA 7, BA 4, A 27, B 48 and E 2 ;

With 20 mM propionic acid (PA) addition, products formed (mM) were AA 1, BA 0, A 20, B 42, E 1 and n-propanol (P) 12.

The proposed biochemical pathways based on the author's stoichiometry for these data are shown in Figs. 20.I, 20.II, 20.III, 20.IV and 20.V.

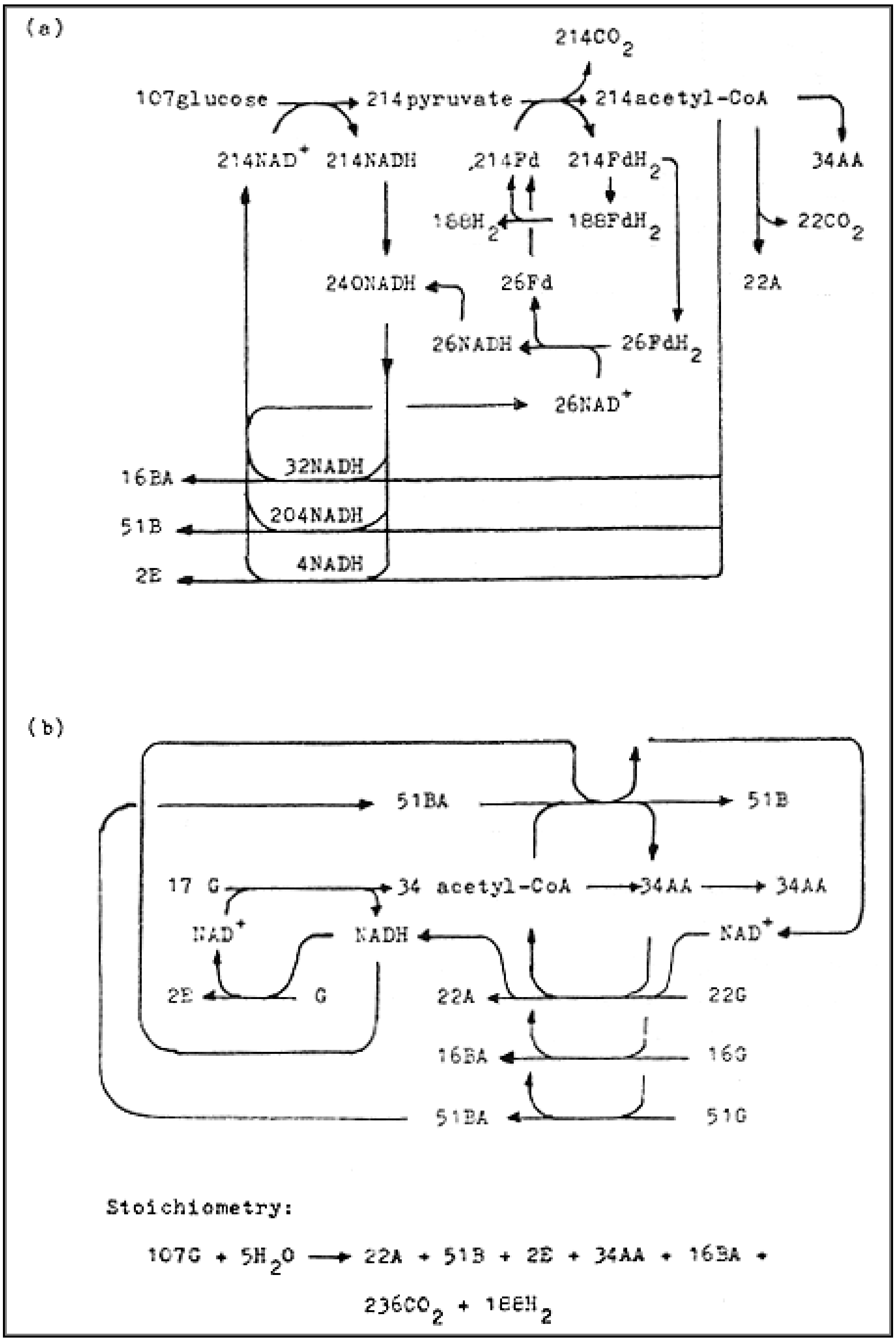
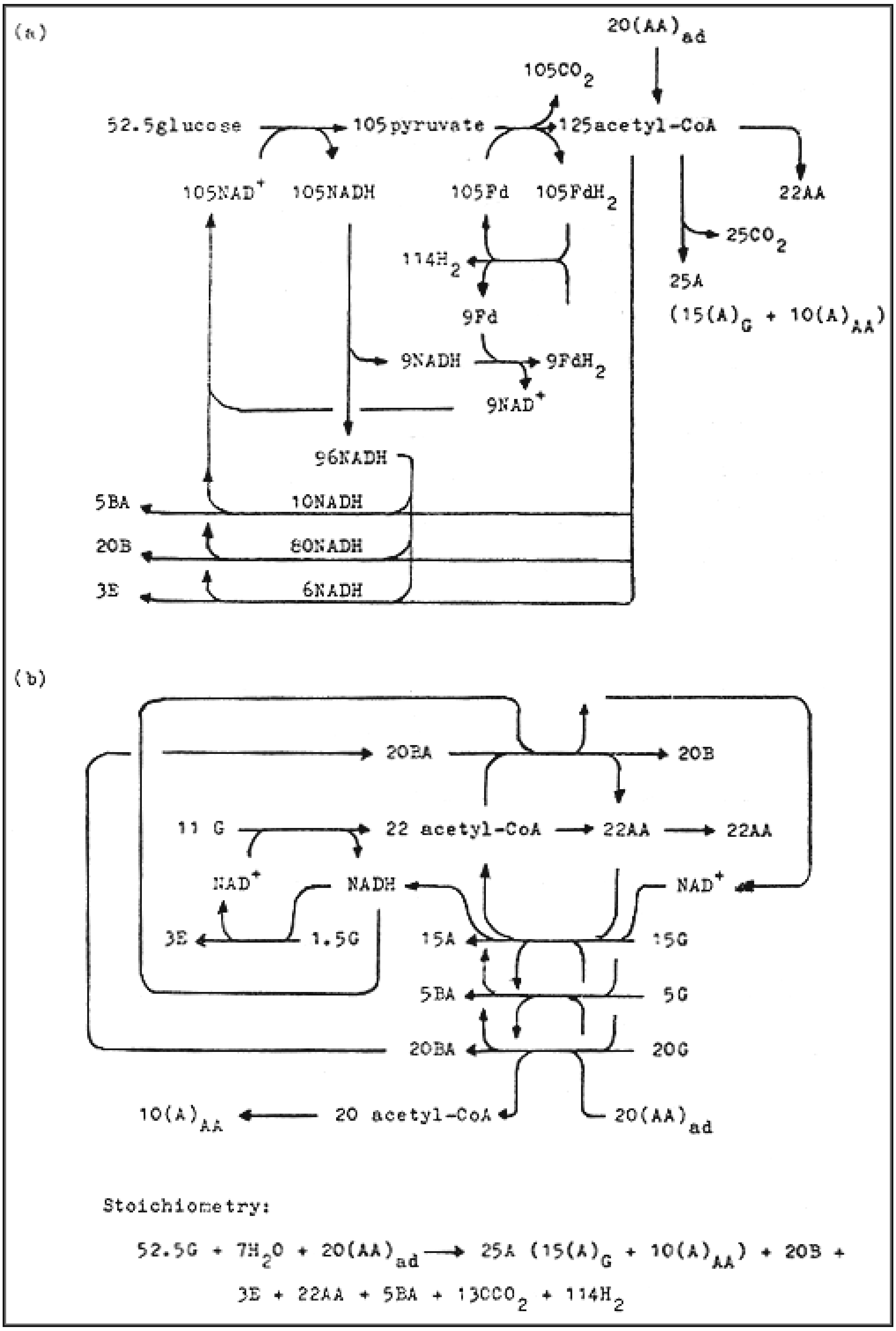


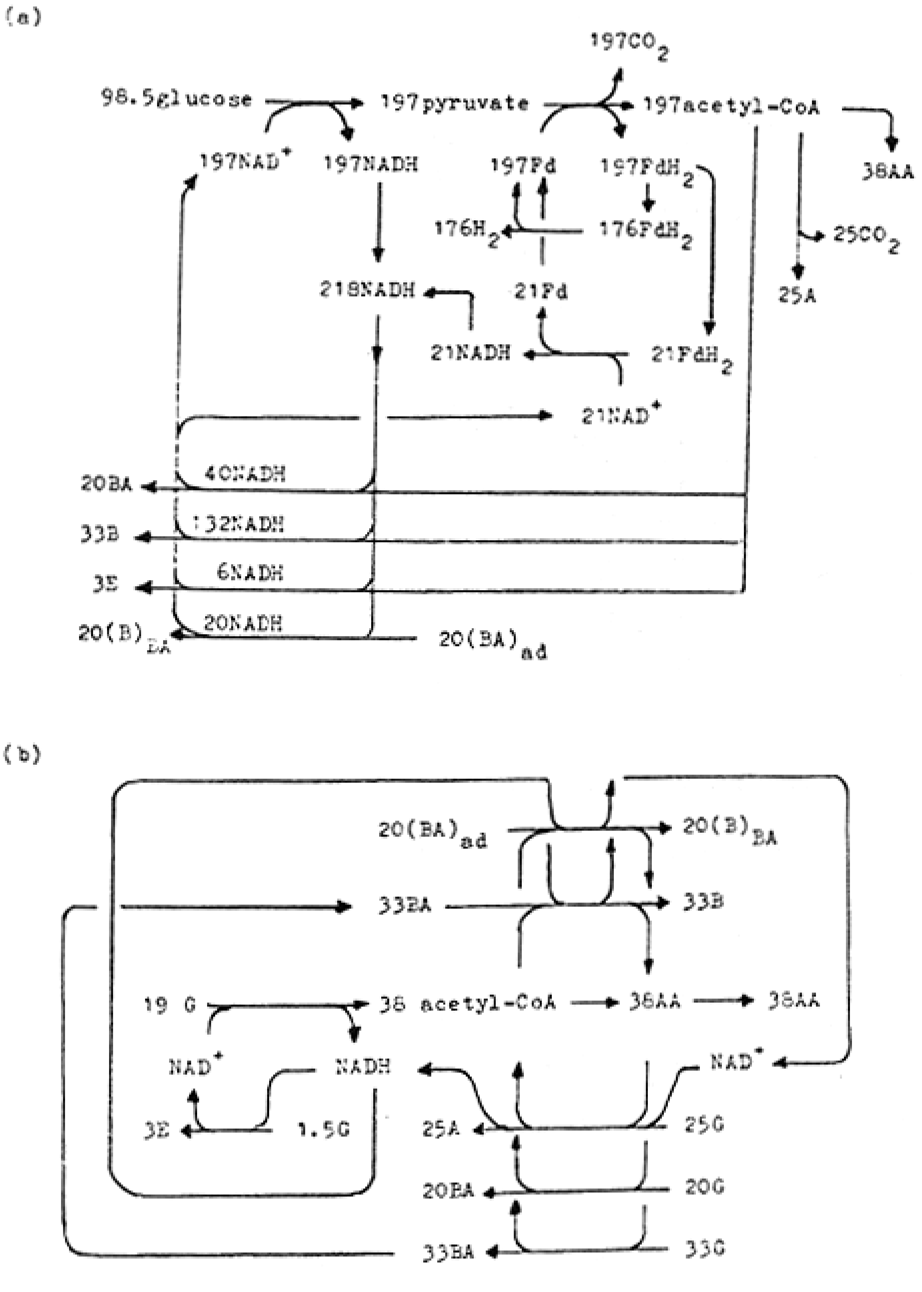
Figure 20.I The author's stoichiometry and proposed biochemical pathways for experimental data from Holt et al 1984, without acid addition :

(a) showing material balance, (b) showing acetate / acetyl-CoA loop.



Figuire 20.II The author's stoichiometry and Proposed biochemical pathways for experimental data from Holt et al 1984, with 20 mM acetic acid addition :

(a) showing material balance, (b) showing acetate / acetyl-CoA loop.



Stoichiometry:

$$98.5G + 10H_2O + 20(BA)_{ad} \longrightarrow 25A + 53B\ (33(B)_G + 20(B)_{BA} + 3E + 38AA + 20BA + 222CO_2 + 176H_2$$

Figure 20.III The author's stoichiometry and proposed biochemical pathways for experimental data from Holt et al 1984, with 20 mM butyric acid addition :
(a) showing material balance, (b) showing acetate/acetyl-CoA loop.

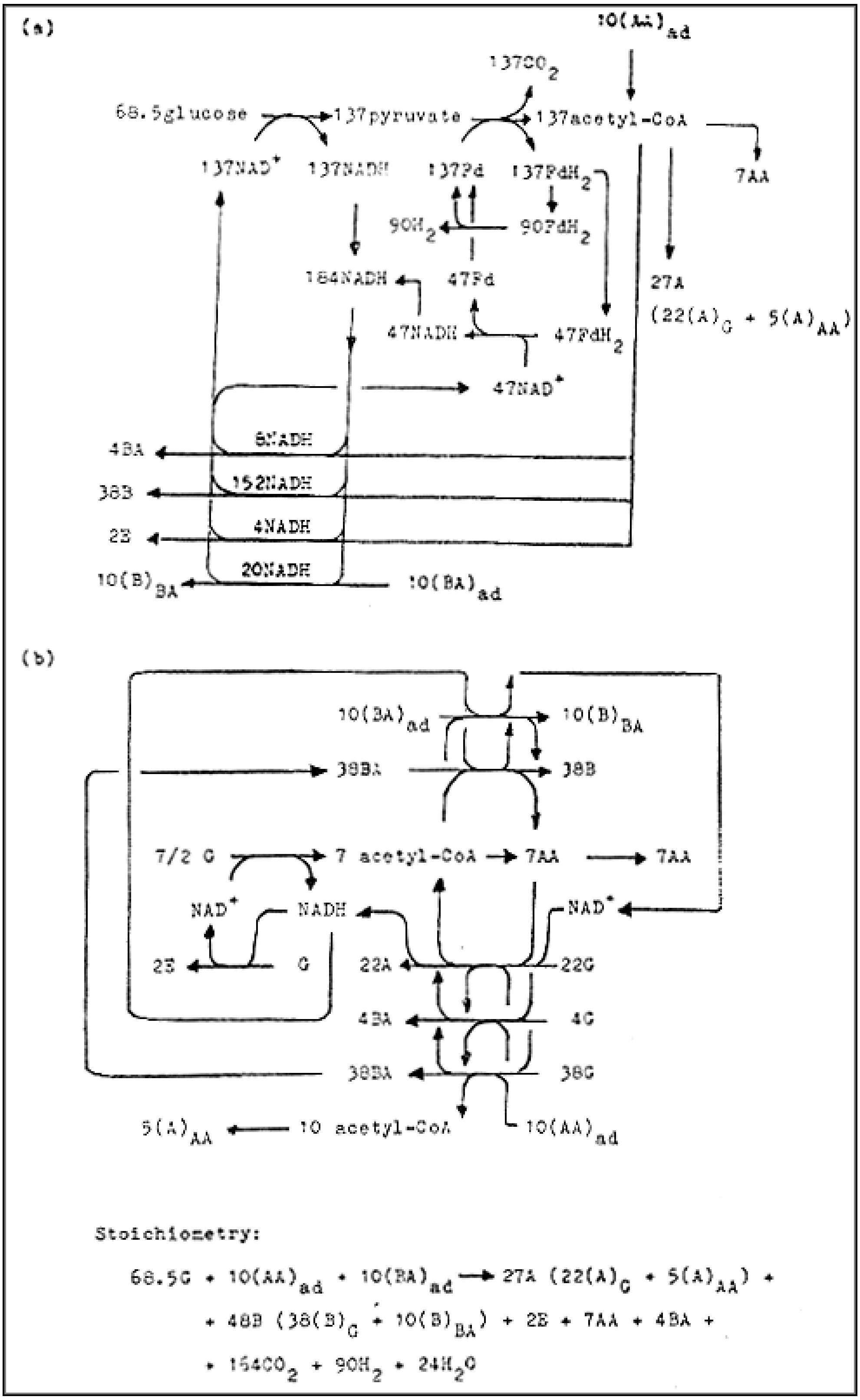


Figure 20.IV The author's stoichiometry and proposed biochemical pathways for experimental data from Holt et al 1984, with 10 mM acetic acid plus 10 mM butyric acid addition : (a) showing material balance, (b) showing acetate / acetyl-CoA loop.

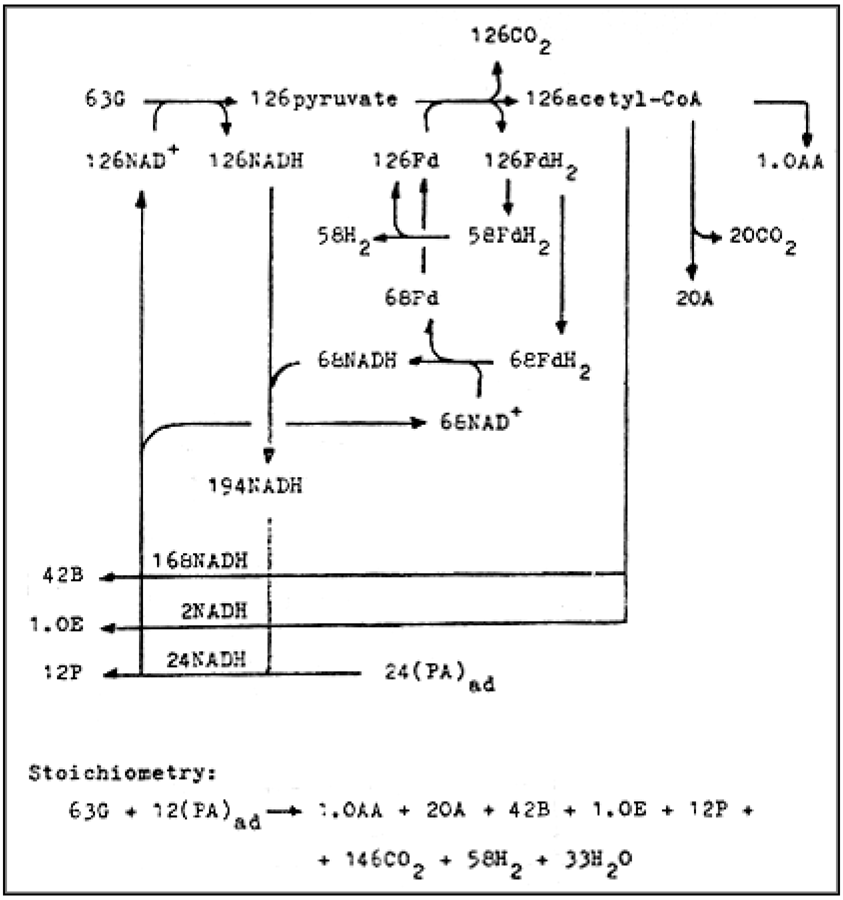


Figure 20.V The author's stoichiometry and proposed biochemical pathways for experimental data from Holt et al 1984, with 20 mM propionic acid addition : showing material balance.

Example 7 Fermentation of glucose with butyrate addition ; data were from Datta and Zeikus 1985 : fermentation vented by CO with 0.10 atm for 72 h ; glucose and butyrate utilized were 51.0 and 4.0 g / l, respectively ; products formed (g / l) were AA 2.3, BA 0.8, A 3.8, B 14.7 and E 1.6.

The proposed biochemical pathways based on the author's stoichiometry for these data are shown in Fig. 21.

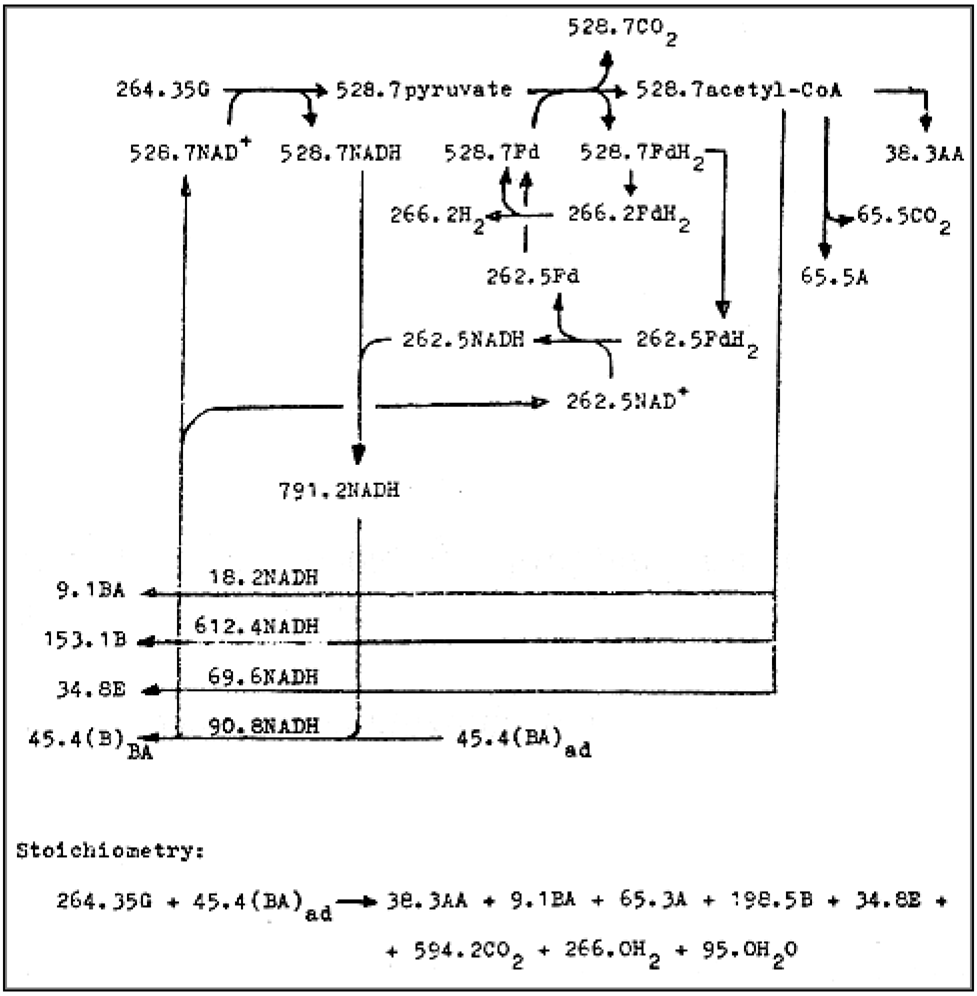


Figure 21 The author's stoichiometry and proposed biochemical pathways for experimental data from Datta and Zeikus 1985 : showing material balance.

Example 8 Batch fermentation of glucose by **C. butylicum** NRRL B592 with butyric acid addition : data were from Pimpa 1982 (Fig. 22) :

Before BA addition, at fermentation time of 26 hours, glucose consumed was 8.61 g/e ; products formed (g / l) were AA 1.98, BA 1.58, A 0.24, B 1.25 and E 0.08 ;

After BA addition, at fermentation time of 91 hours, glucose and butyrate consumed were 26.7 and 3.35 g / l, respectively ; products formed (g / l) were AA 2.76, BA 2.12, A 2.12, B 8.00 and E 0.14.

The proposed biochemical pathways based on the author's stoichiometry for these data are shown in Fig. 23.

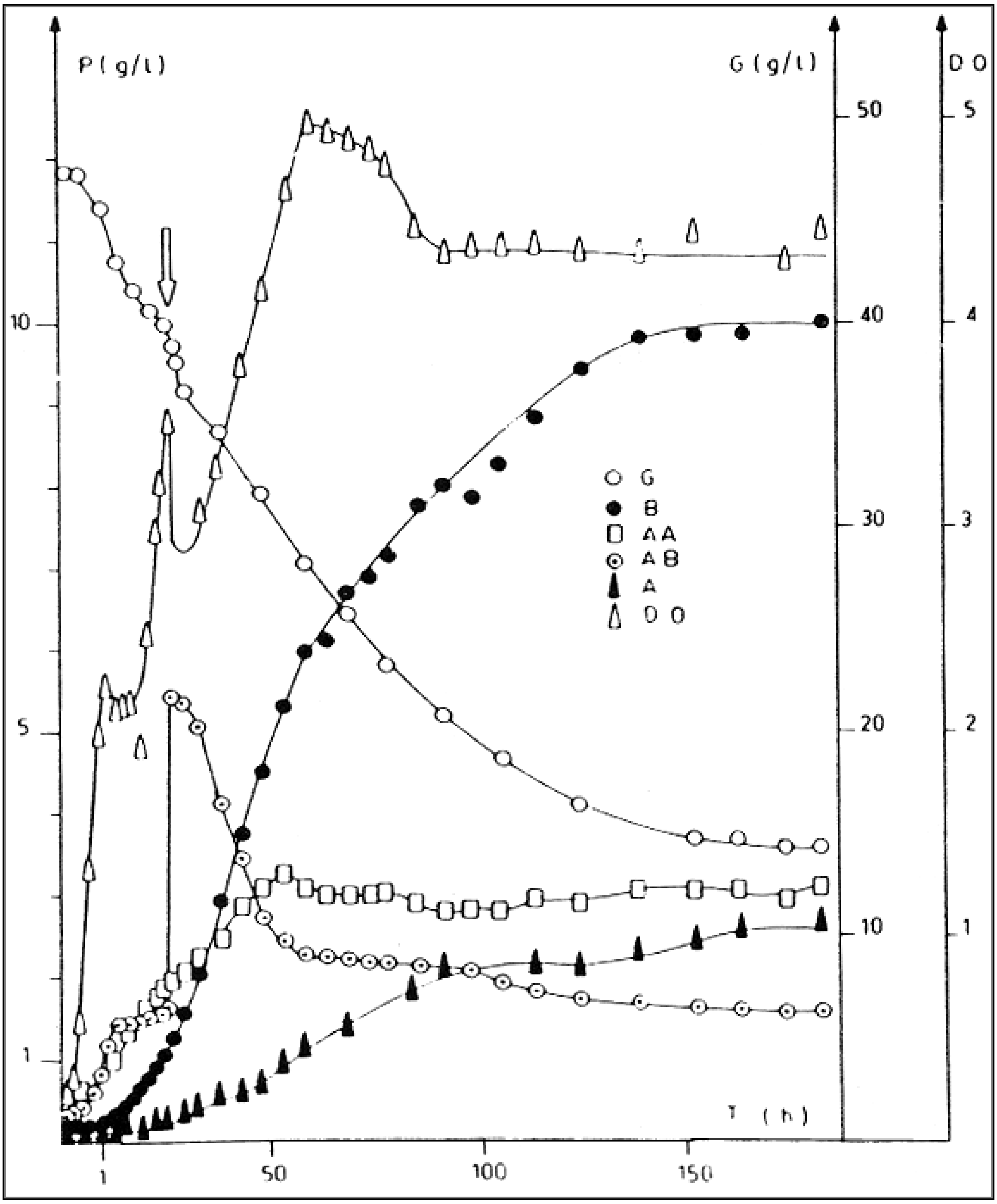


Figure 22 Batch fermentation of glucose with butyric acid addition by **C. butylicum** NRRL B592, data were from Pimpa 1982. Symbols used are as follows :

P = Products, G = Glucose, B = Butanol, AA = Acetic Acid, AB = Butyric Acid, A = Acetone, DO = Optical Density and T = Time.

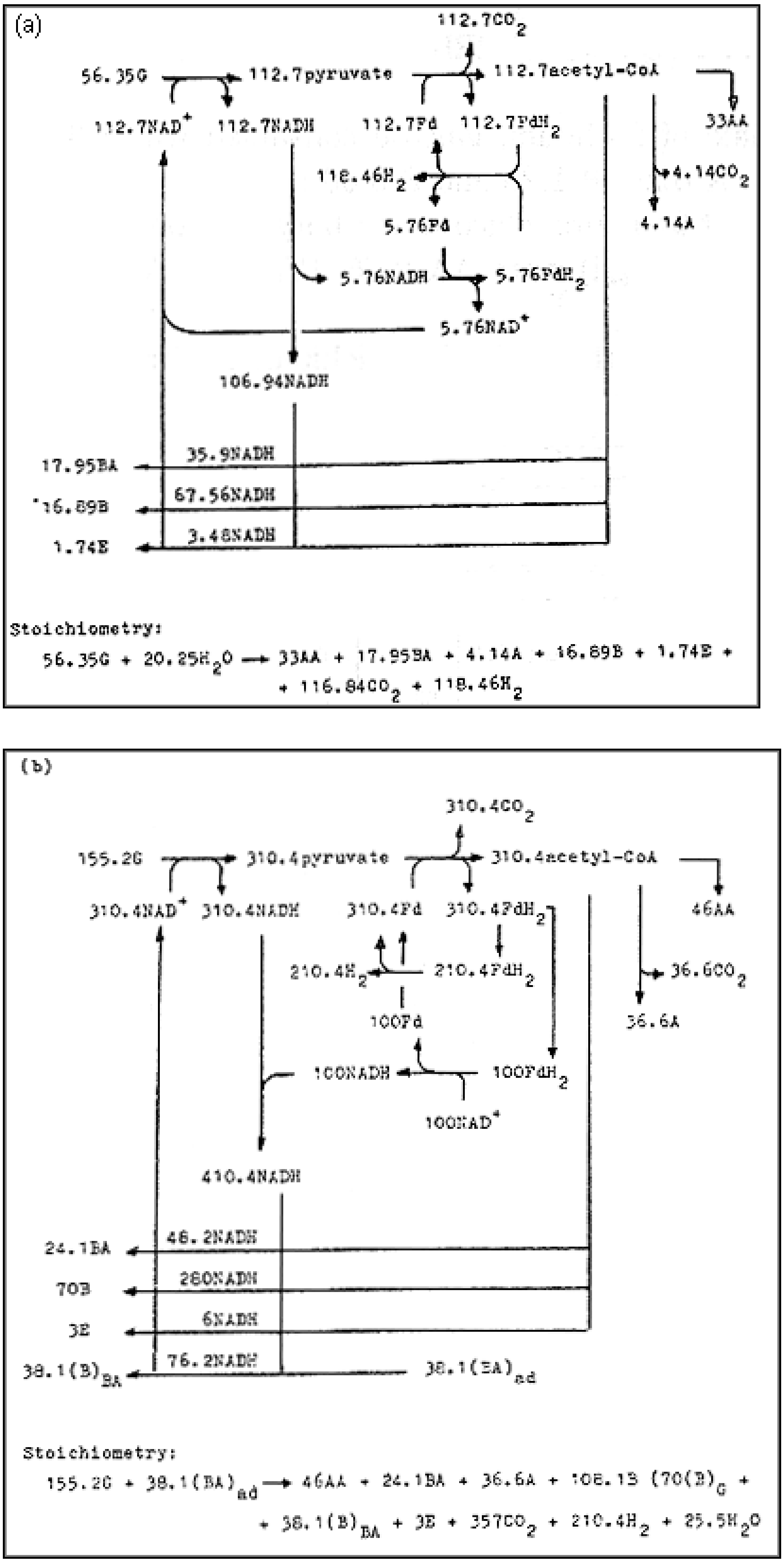


Figure 23 Stoichiometry, and proposed biochemical pathways for experimental data from Pimpa 1982 : showing material balance, before butyric acid addition (a), after BA addition (b).

Example 9 Solvent production by **C. acetobutylicum** with pyruvate addition ; data were from Ballongue et al 1986 (their Table 4) : glucose and pyruvate used were 15 and 1.5 g / l, respectively ; products formed (g / l) were AA 7. 1, BA 5.1, A 0.4, B 3.2 and E 0.2.

The proposed biochemical pathways based on the author's stoichiometry for these data are shown in Fig. 24.

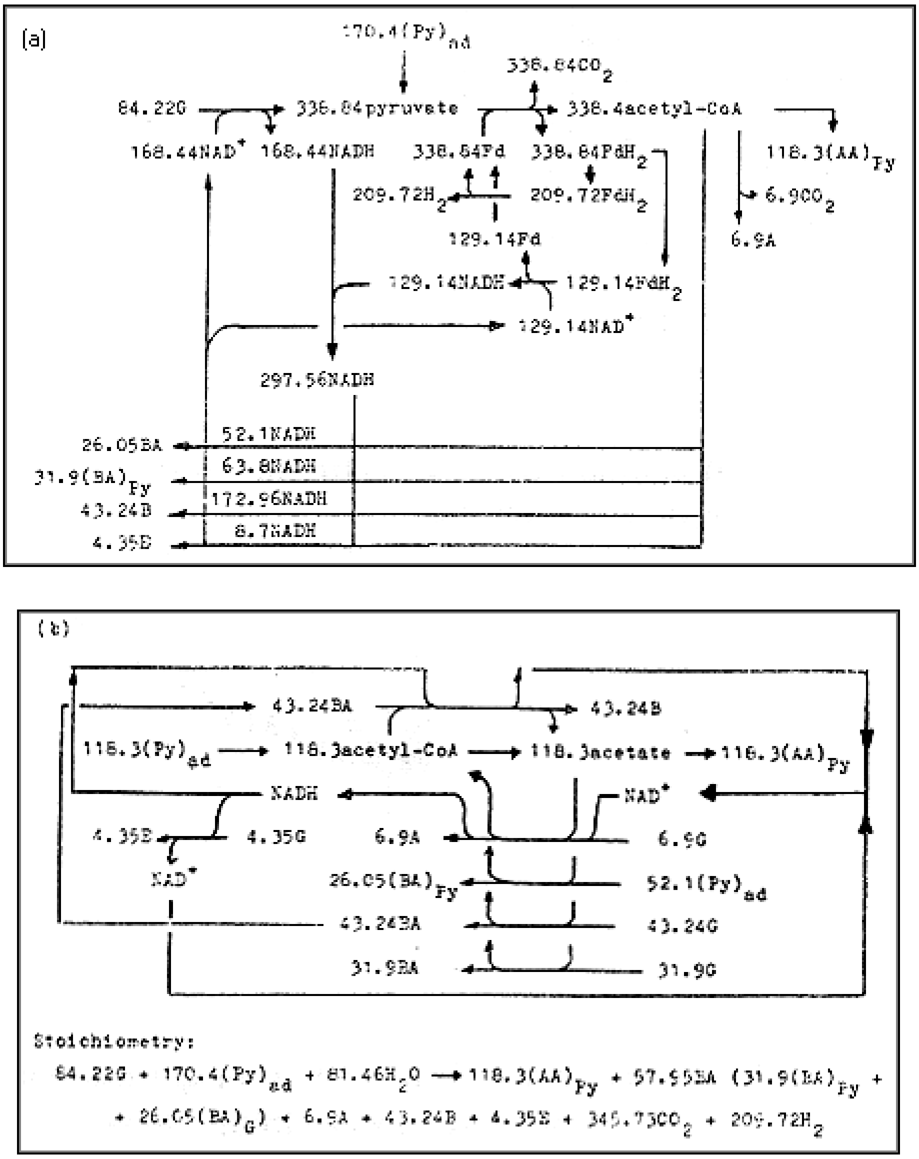


Figure 24 The author's stoichiometry and proposed biochemical pathways for experimental data from Ballongue et al 1986 :

(a) showing material balance, (b) showing acetate/acetyl-CoA loop.

4. REFERENCES

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