Supplementary Table S1. List of primers used in RACE and cloning of PEPCK from *R. echinobothrida.*

Primer*	Primer sequence 5'→3'
PCK_FP(D)	GATCCCAAAGATGTTGCTCGTGTCG
PCK_RP(D)	GCGGCGGTAGCCTCGGATTT
GSP_PCK_FP	CCTGGCTGCATGAATGGCCGCAC
GSP_PCK_RP	GGAGCGACACCGAAGAAGCCCGC
3'-RACE	AAGCAGTGGTATCAACGCAGAGTAC$(T)_{30}$VN
5'-RACE	$(T)_{25}$VN
LD_PCK_FP	GAGGAGAAGTCGACTAAGCCCAAGCC
LD_PCK_RP	TTGGGAAGAGCGGCCGCAACTTGGT
pE_PCK_FP	AACACGTCTCAAGGTATGTCGCCAACTCTTTGG
pE_PCK_RP	GGCGCTCGAGTTACATTGCTTTAATGCG

*PCK: PEPCK; D: Degenerate; FP: Forward primer; RP: Reverse primer; GSP: Gene specific primer; LD: Long distance; N: A, C, G, or T; V: A, G, or C; underlined sequences of pE_PCK_FP and pE_PCK_RP primers show the restriction cut sites, BsmB1 and Xho1, respectively.

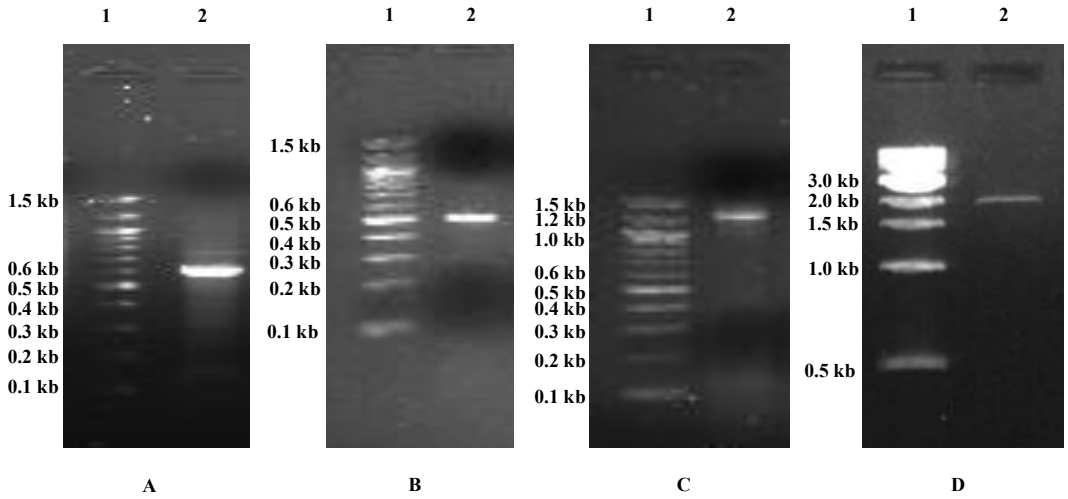
Supplementary Table S2. VADAR (Volume, Area, Dihedral Angle Reporter) statistics of modelled PEPCK from *R. echinobothrida* and rat cytosolic PEPCK Ld_3g in complex with PEP and GDP (PDB ID 4GNP). The web server (http://vadar.wishartlab.com) was used for quantitative evaluation of protein structure quality.

Statistics	Observed (PEPCK model)	Expected (PEPCK model)	Observed (PDB ID 4GNP)	Expected (PDB ID 4GNP)
Residues in phipsi core	567 (91 %)	558 (90 %)	554 (91 %)	545 (90 %)
Residues in phipsi allowed	43 (6 %)	43 (7 %)	48 (7 %)	42 (7 %)
Residues in phipsi generous	6 (0 %)	6 (1 %)	1 (0 %)	6 (1 %)
Residues in phipsi outside	4 (0 %)	0 (0%)	2 (0 %)	0 (0%)
Residues in omega core	591 (95 %)	595 (96 %)	542 (89 %)	581 (96 %)
Residues in omega allowed	23 (3 %)	19 (3 %)	42 (6 %)	18 (3 %)
Residues in omega generous	4 (0 %)	0 (0 %)	15 (2 %)	0 (0 %)
Residues in omega outside	2 (0 %)	6 (1 %)	6 (0 %)	6 (1 %)
Packing defects	82	43	74	42
Free energy of folding	-621.23	-597.78	-610.29	-582.93
Residues 95% buried	227	278	229	269
Buried charges	24	0	12	0

Supplementary Table S3. Predicted interactions of substrate, cofactors and possible modulators with PEPCK from *R. echinobothrida*. The amino acids in bold obtained using DS 4.1 (Accelrys-Biovia) participate in the active site of PEPCK.

Substrate/ cofactors/ modulators	Predicted interacting amino acids	CDocker energy (kcal/mol)	H-bonds	RMSD value* (PDB ID)
PEP	**R90, G243, N411, R413**	-88.6	5	0.22 Å (4GNP), 0.36 Å (4GMW)
Mn (M1)	**K250, H270, D317**	-	-	-
GDP	**A293, G295, K296, T297, N298, F537, N540**	-81.5	9	0.22 Å (4GNP), 0.36 Å (4GMW)
THP	**A293, C294, F524, F537, N540**	-51.3	4	NA
Genistein	R444, **F524, F537**	-46.1	0	NA
PZQ	**W523, F524, F532, F537, N540**	-30.5	2	NA
Daidzein	I116, Q119, R255, R491, P492	-8.5	2	NA

*RMSD value was obtained by superimposing the docked structure upon the available crystal structure complexes from the Protein Data Bank (www.rcsb.org/pdb). PDB ID **4GNP**: rat cytosolic PEPCK Ld_3g in complex with PEP and GDP; PDB ID **4GMW**: rat cytosolic PEPCK Ld_1g in complex with PEP and GDP; NA: not available.



Supplementary Fig. S1. 5'- and 3'-RACE were performed in order to obtain the ORF of PEPCK from *R. echinobothrida*, and analyzed on 1.2 % agarose gel. (A) Amplification of core amplicon: lane 1. 100 bp DNA ladder; lane 2. 627 bp core amplicon of PEPCK. (B) 5'-RACE product: lane 1. 100 bp DNA ladder; lane 2. 457 bp amplicon. (C) 3'-RACE product: lane 1. 100 bp DNA ladder; lane 2. 1130 bp amplicon . (D) ORF of PEPCK: lane 1. 1 kb DNA ladder; lane 2. 1887 bp amplicon of ORF.

ACATGGGACACACGCAAACTTTCCGCTCGTA**ATG**TCGCCAACTCTTTGGACTGAGGAGAAGTCGGTCAAGCCCAAGCCTCCTTTTGTTAAAGGACGTTTCGAAGACC
TTCCTGCTGTGGTGCAGCCTTTCGTTGCTCACTGGGCTAATGTCTGCACACCAAAAGACGTCTTCATCTGTGATGGTAGCAAGGCTGAGGCCGATGCCATTACTGAT
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TACGTTGTGCTTTGCATGCGTATCATGACACGCATGTCACCGAAAGTATTCGATTACATTAAGGAGCAAAACGCCTTTGTGCGTTGCGTTCACTCTATCGGGTTGCC
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GATATGGTGGCAACTCACTCCTTGGCAAGAAATGCTTTGCCCTACGTATTGCCAGCCGTATTGCCTATGATGAAGGCTGGATGGCTGAACACATGCTTATCATGTCT
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GAGACCACTAAATTCCTTGATGACCAAGTTGGACCCGATCTTCCCAAGGAGATTAAGGAAGAATTAGCCAATCAATTGAATCGCATTAAAGCAATG**TAA**AACCCAAA
GGGCTTTTCATAATCGGGCTTATCCCAAAAAAACAATTTAGCTTTTATGTTACCCCACCTTCGATTTGTCTTTTTCCAGCATTTCACTTATCACATTTTCCAAACCT
TCCCTTTTTTCACCTATTTGGTAAAATTAGTCGTGTTACTTAAATCTCCCTTCGGTCATGATGACCAATCCTTTTTCACTCCTTTCAACGCAAAGTACGATGTAGTA
TTTTTTTTCCGTGTTTTCACTGCTTG

A

MSPTLWTEEKSVKPKPPFVKGRFEDLPAVVQPFVAHWANVCTPKDVFICDGSKAEADAITDDLLKSGTLRRLAAYENNYICCTDPKDVARVESKTFISTPEKYQTVPHAAEGV KGILGQ
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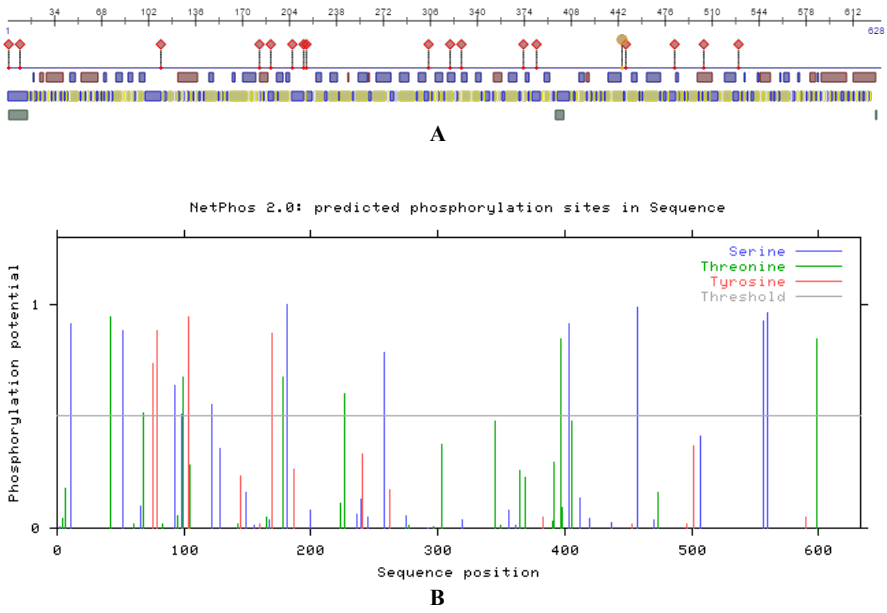
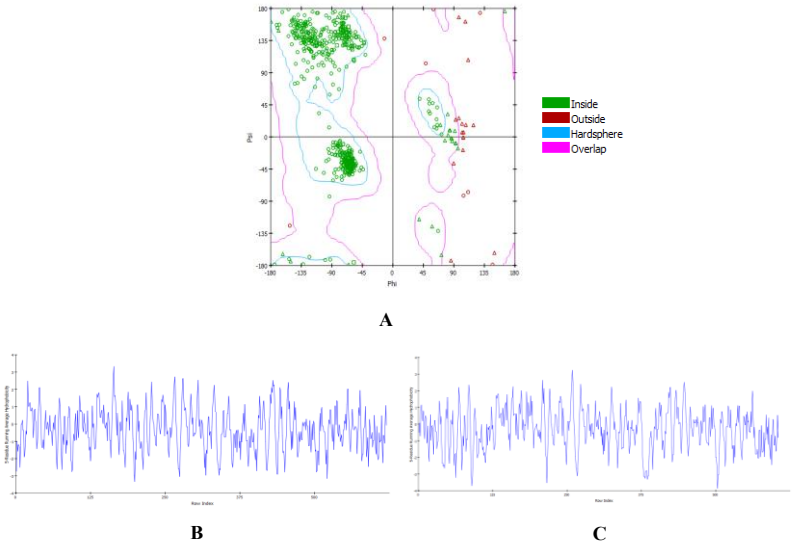
EETTKFLDDQVGPDLPKEIKEELANQLNRIKAM
'

B

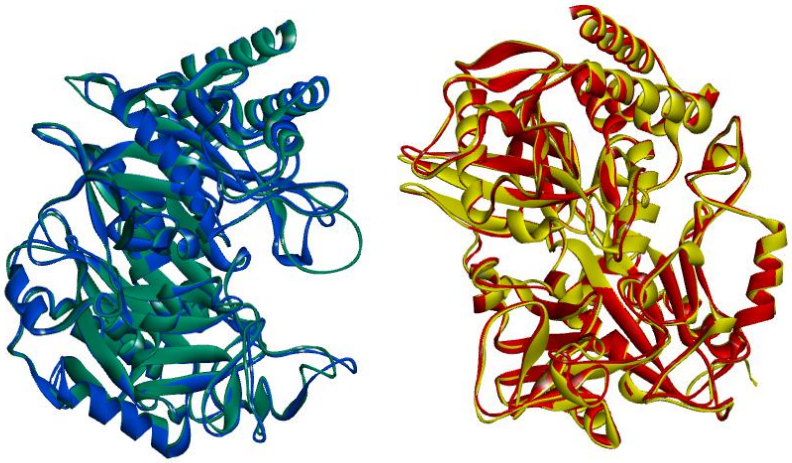
Supplementary Fig. S2. Nulceotide and amino acid sequences of PEPCK from *R. echinobothrida*. (A) The full length of the gene (NCBI GenBank acc. no KC252609.1) contains 2166 bp with an ORF of 1884 bp (shown in red colour). (B) Translated ORF of PEPCK using ExPASy Translate tool (http://web.expasy.org/translate/).



Supplementary Fig. S3. Predicted secondary structures and phosphorylation sites of PEPCK from *R. echinobothrida*. (A) Secondary structures of the protein were predicted using Predict Protein server (https://www.predictprotein.org/). The pink diamond shapes in second row show predicted active sites. Blue and red colours in the third row represent β-sheets and α-helix, respectively; blue and yellow colours in the fourth row show exposed and buried regions, respectively; and the fifth row shows the disordered regions of the sequence. (B) Phosphorylation sites of PEPCK, predicted using NetPhos 2.0 Server (http://www.cbs.dtu.dk/services/NetPhos/) with high confidence values.



Supplementary Fig. S4. Validation of PEPCK model from the parasite using DS 4.1. (A) Ramachandran plot for the PEPCK from the parasite was analyzed using RAMPAGE (Ramachandran Plot Assessment Program) (http://mordred.bioc.cam.ac.uk/~rapper/rampage.php) and DS 4.1. The plot shows that 96.6% residues are found in the most favoured regions (green colour). Hydrophobicity plot for PEPCK from the parasite (B) was compared with its template model (C). The values shown on the X-axis reflect the average hydrophobicity of the proteins with the corresponding amino acids and their score is shown on the Y-axis.



A B

Supplementary Fig. S5. Validation of modelled PEPCK from the parasite. (A) Structural alignment of the models generated from DS 4.1 (in green colour) and Swiss Model (in blue colour) shows RMSD value of 0.75 Å. (B) Structural superimposition of the modelled PEPCK from the parasite (in yellow colour) with its host PEPCK (chicken mitochondrial PEPCK; PDB ID 2FAF, in red colour), showing RMSD value of 1.05Å.